THE
VETERINARY JOURNAL

Editorials

ANIMAL IMMUNITY.

THE discovery of a successful method for the treatment of a disease, when the latter has become definitely discovered, is one thing, but its prevention by scientific means is equally valuable—or, perhaps, of even more value—and in this issue we are pleased to be able to announce to our readers the good news that three more of the scourges of our animal patients—viz.: canine distemper, ferret distemper and lamb dysentery—have received such successful attention that their respective prophylaxis and control appear to be within measurable distance.

The scientific research work on distemper, originally started at the request of THE VETERINARY JOURNAL, and carried out by the Medical Research Council with money generously collected and given by the "Field" Distemper Fund, has been brought to a satisfactory conclusion, inasmuch as it has been demonstrated beyond question that dogs can now be inoculated satisfactorily against distemper. For this brilliant result the veterinary profession (although in the earlier stages of the research the names of Dr. Gye, M.D., Mr. Barnard and Mr. Glover, M.R.C.V.S., figured largely) had mainly to thank Dr. P. P. Laidlaw, a well-known medical bacteriologist, and Major G. Dunkin, M.R.C.V.S., D.V.H., the Veterinary Superintendent of the Mill Hill Laboratories. It is a triumph for these two workers, and a triumph which the late Sir Theodore Cook, the generous Editor of the "Field," and his colleague Dr. Hammond Smith, would have rejoiced in had they been spared to share in it; for there can be no doubt that had it not been for the practical encouragement and generous help of the former, together with the clever propaganda appeals issued by the persevering Secretary of the Fund, Mr. Moss-Blundell, the money would not have been forthcoming, and this Research could not have been done.

The number of so-called specifics and quack nostrums against distemper which are on the market is legion, and the fact that their respective proprietors can afford to pay large sums for advertising space tells its own tale as to the monetary profit made; whilst there is not one which is universally accepted by the members of the

veterinary profession in this or any other country as being of really certain and effective help—even as an adjunct.

By the research of Messrs. Laidlaw and Dunkin a prophylactic method has been worked out whereby puppies of all breeds can now be immunized against distemper and the vaccine will shortly be able to be obtained by medical men and veterinarians from the Wellcome Laboratories (where there are three veterinary graduates on the scientific staff). The first dog was immunized rather more than two years ago, and has remained immune; and since then we read that 1,330 dogs and 325 couples of foxhounds "have been treated in the course of the investigations, with very satisfactory results."

When this can be followed up by a further announcement that a certain specific "*curative*" treatment has been equally definitely established, the gratitude of the canine world, and of those whose life's work is to treat and nurse dogs in illness, will indeed be boundless. We publish the technical report in full and commend its perusal to our readers.

Of equal service to the country in general, and to the Agricultural World in particular, is the work which has been done, during the past ten years, upon certain sheep and lamb diseases which have devastated our flocks and herds for many years almost unchecked. In fact to such a pretty pass had things come that sheep breeding and lamb rearing had become almost an impossibility in certain districts. In the category of research workers on these sheep diseases the names of Professor Gaiger, F.R.C.V.S., now of Liverpool University, Major Dalling, M.R.C.V.S., of the Wellcome Laboratories, and Mr. Arthur Pool, M.R.C.V.S., Director of the Animal Diseases Research Association, stand out pre-eminently, and it is to an article in this December number on "Lamb Dysentery Prophylaxis in 1928," by Messrs. Dalling, Mason and Gordon, M.R.C.V.S., that we would particularly draw attention. In this article Major Dalling gives full details of work which has been done during the lambing seasons of 1927-28, and records tables showing the proportion of deaths amongst animals inoculated and uninoculated respectively; concluding his summaries with the very gratifying and satisfactory statements that—

> "Toxoided" whole culture of the lamb dysentery anaerobe used as a vaccine for ewe inoculation yields a high degree of protection against lamb dysentery in lambs"; and "antitoxin of the lamb dysentery anaerobe injected into young lambs prevents lamb dysentery in at least 99 per cent. of cases."

This claim, like that of the prophylactic against canine distemper, is made as the result of original research, and the successful sequel in each case should make the dog owner and the sheep breeder equally

realise the debt of gratitude which they owe to veterinary science; a debt which should be repaid by loyal support, pecuniary and otherwise, on every possible occasion. In other countries whose wealth depends upon the value of its animals, the fact that those animals must be kept free from epidemics is fully recognised, and those in authority are cognisant that the only man who can help them effectually is the qualified veterinarian. The way in which rinderpest is controlled in South Africa is one of the best illustrations of the value of a practical application of scientific veterinary knowledge; and even in our own country the simple present-day preventive treatment of blackquarter (as instanced by an outbreak reported on page 648) takes us far ahead of the helpless days in which our forefathers used to be resigned to the loss every year of a certain proportion of their calves and young stock, usually the best of the herd. *It is the monetary problem which has kept veterinary research in the background in the past, and the young graduates of the profession are badly in need of more encouragement in the way of scholarships and bursaries to enable those who are fitted for this kind of work to follow it up and so to add the results of their efforts to the sum total of what is being done for the alleviation of animal suffering.*

THE TOTALISER AND VETERINARY RESEARCH SCHOLARSHIPS.

THE Special Commissioner of the *Sporting Life* has made public in a recent issue (December 7th) a suggestion brought forward by Mr. C. Edmunds, the Manager of the Mentmore Stud, at the Newmarket meeting of the Thoroughbred Breeders' Association, "that some at least of the surplus profits from the Totaliser (if and when there is any) should be applied to the foundation of scholarships for young veterinary surgeons, who are prepared and equipped to devote themselves to research work in connection with the diseases of animals in general and horses in particular."

The suggestion is one which, if adopted, would be welcomed by the veterinary profession, and especially by the young graduate who is attracted by research work. At the present time, in by far the majority of cases, the financial outlook for the laboratory and research worker in this country is such an unsatisfactory one, not only at the commencement of his career, but also in regard to its future, that he is forced to take up one or other of the branches of the profession which offer better financial prospects.

The Special Commissioner (who, by the way, promises to "deal at length with this question shortly") writes in a further paragraph.

"in the meantime I must congratulate Mr. Edmunds on his revolutionary suggestion—revolutionary in that it would make the veterinary profession a more attractive one than it is and would put the treatment of diseases of the horse upon a better footing." It is a note of kindly sympathy from one sporting section of the community to another, and we hope that it will speedily take some practical shape; and that if its fulfilment depends on the adoption of the Totaliser, the arrival of that machine (bone of contention though it may be) will not be delayed.

THE COLONIAL UNDER SECRETARY AND THE VETERINARY SERVICES.

In a speech delivered on December 6th by Mr. Ormsby-Gore, M.P., Parliamentary Under Secretary of the Colonies, at a public meeting arranged by the Association of Scientific Workers and held at University College, Mr. Ormsby-Gore chose as the title of his address, "Developments and Opportunities in the Colonial Empire," and after alluding to the various departments of which the Colonial Government Service is composed he spoke of the Agricultural and Veterinary in the following terms: the headlines in the *Times*, in large type, being "Veterinary Services Behindhand."

VETERINARY SERVICES BEHINDHAND.

> "The number of agricultural officers had risen from 11 to 42, and to this last figure must be added a further 15 agricultural scholarships. He regretted to say that the veterinary services were still much behindhand. They appointed seven in 1913 and only nine in 1927. In the whole Colonial Empire they had at the present moment only 127 veterinary officers, including specialists, yet there were something like 10,000,000 head of cattle, besides other domestic animals."

Possibly the heading was not intentionally reproachful towards us—for it can be taken in two ways—and we venture to think that the fact of the veterinary services being "behindhand" alludes to the paucity of new appointments which were made in 1927-28. This is a matter for the Colonial office to remedy; and, as it is stated that there are only the astonishingly small number of "127 veterinary officers, including specialists, in the whole Colonial Empire," whilst the cattle population for whose freedom from epidemics they are responsible number some 10,000,000, it is really a matter of wonderment how our colleagues manage to keep control at all. It is to their credit, but we should like to see their work better appreciated both as regards help, pay, study leave and pension.

General Articles

THE PREVENTION OF DISTEMPER. DISCOVERY OF AN IMMUNITY VACCINE.

Preface.

THE "Field" Distemper Council and the Medical Research Council have received from the Distemper Research Committee the following Report, including a statement by the investigators of the whole of their work during the past five years in the study of the cause and prevention of dog distemper. This report both Councils have adopted, and they now accordingly present it to the public.

The whole work of scientific investigation described in the following pages has been conducted for the Distemper Research Committee by Dr. P. P. Laidlaw and Mr. G. W. Dunkin, both in the service of the Medical Research Council. The heavy cost of the special buildings required for animal accommodation, the services of kennel-maids and other assistants, and all expenses directly incurred in this work have been provided from the voluntary contributions to the Fund raised by the "Field" newspaper and administered by the "Field" Distemper Council. The site for the work, laboratory accommodation, and other technical facilities have been provided by the Medical Research Council at the Farm Laboratories of the National Institute for Medical Research, near Mill Hill, Middlesex.

It will be observed from the Report that this work has added securely to our knowledge of the causation of the disease, and it has already also brought a most satisfactory measure of practical success in the prevention of distemper in ferrets and dogs. The knowledge and experience gained will certainly have a wider value, as indeed events have already proved, for the study and control of virus diseases in general among men and in other animals. Upon these results, both scientific and practical, the investigators are to be warmly congratulated. It is hoped that by arrangements already in hand the immediate benefits of this work will very soon be made generally available for

XUM

the owners of dogs. The investigators, however, are confident that further improvement and simplification in the methods of immunizing dogs can be attained, and for that reason it is highly desirable that the researches should continue for another year or two. The " Field " Distemper Fund (Windsor House, Bream's Buildings, London, E.C.4) will accordingly remain open for further subscriptions from the public, which has in the past so generously supported this important work.

PORTLAND,
President, " Field " Distemper Council

BALFOUR,
Chairman, Medical Research Council

London.
November 24th, 1928.

A REPORT UPON THE CAUSE AND PREVENTION OF DOG DISTEMPER.

By P. P. LAIDLAW, B.Ch., F.R.S., and
G. W. DUNKIN, M.R.C.V.S., D.V.H.

To the " Field " Distemper Council
and the Medical Research Council.

FOR the purposes of the progress report now submitted, the Research Committee have departed from their usual procedure, followed in each of the seven interim reports previously submitted, of reviewing only the work done since the last occasion. They have asked Dr. P. P. Laidlaw and Mr. G. W. Dunkin, who have for the past five years undertaken the investigation and to whom must be attributed all the success which has been achieved, to prepare a general account of their researches from the beginning. This summary by the investigators is accordingly submitted herewith.

The reason which has led the Committee to adopt this course is that the investigations have reached a point when the knowledge acquired is capable of being usefully applied in practice to rendering dogs resistant to infection by distemper. This has been demonstrated beyond peradventure by experiments at the Farm Laboratories during the year, and trials made with sporting and other dogs under ordinary conditions have so far supported the conclusions of the laboratory experiments.

The Method of Immunization.

The method consists of a double inoculation. The first inoculation is made with a vaccine which is, in fact, the inactivated virus of distemper. The second is made, after an interval of about 10 days, with an attenuated strain of living virus. The dose of living virus is a hundredfold that which would infect a dog not previously treated with the vaccine, but as a rule it is followed by nothing more than a trivial and transient disturbance of health: often no departure from the normal can be detected. Dogs which have undergone this double inoculation have proved to be completely resistant to the disease thereafter, whether exposed to infection by being placed in close contact with animals suffering from the disease or by the administration of infective material.

The method of preparing the vaccine is not yet ideal, and the dosage of the vaccine and of the subsequently given living virus can be undertaken only by skilled hands. But until artificial cultivation of the virus, outside the animal body, has been achieved, these difficulties are not likely to be completely removed, although important improvements in the technique of manufacture and of administration will surely be discovered in the course of further experience.

In the meantime, the preparation of the materials is difficult and calls for great skill, while for the administration of the vaccine and virus the services of a veterinary practitioner are desirable.

Large-Scale Vaccine Production.

It follows from what has just been said that the vaccine cannot be made without first-class laboratory resources and equipment, and the question arises as to how dog-owners can now be provided with the means of preventive treatment which scientific experiment has shown to be useful.

It is clear that the manufacture and distribution of vaccine on a large scale cannot be undertaken by the investigators. Such operations are not the function of a research laboratory, and they call for an organisation of another type and for resources of a different order. At various stages in the course of the investigations, experimental batches have been issued for trial by dog-owners under ordinary conditions; the quantities available have necessarily been small, and the distribution has been made solely with a view to obtaining evidence useful to the work of research. Now, however, that there is justification for bringing the method into general use the work of vaccine production must pass to other hands. This is necessary not only in order that large-scale production may be achieved, but also

in order that the investigators may be left unembarrassed in their further research work for the improvement of the method.

In this regard it may be noted that the methods of preparation and administration have already been made public. In accordance with customary scientific practice, the investigators have published details of their results, stage by stage, in a series of papers communicated to an appropriate scientific journal. (References to those papers are given at the conclusion of the appended report.) It is, therefore, open to commercial firms in this and other countries to develop the production of the vaccine with a view to placing it on the market, while the absence of any monopoly should safeguard the public in respect of the price charged.

The Committee realise, nevertheless, that indiscriminate manufacture might result in the marketing of inferior preparations, which would inevitably lead to disappointment and tend to bring the method into undeserved discredit. They have accordingly thought it well, as regards Great Britain, to invite a well-equipped commercial laboratory to undertake the work, and to offer it at the outset such technical advice and assistance (as, for instance, in the standardisation of the product) as may be helpful. Similar facilities would, of course, be placed at the disposal of any other laboratory or institution desirous of taking up production, provided that the Committee were satisfied that the necessary experience and equipment were available.

Continuance of the Research Work.

Finally, there is no reason to suppose that the investigators who have made steady progress to this point have necessarily reached the limit of their achievement, and that this first practical fruition is the final harvest of the work. There remain several possible lines of investigation along which some improvement of the method may be sought, and it is therefore proposed that the research work should continue for a further period.

There is, for instance, little doubt that the complete solution of the problem of distemper prevention demands the cultivation of the virus apart from the living animal. This has so far baffled the ingenuity of the investigators. Nor, in general, have those working at other virus diseases, here or in other countries, yet been more successful; but the solution of the problem in any one case is not unlikely to point the way to its solution in others. The investigators are, therefore, continuing their efforts to grow the virus of distemper in artificial media.

Another line of research which is still being pursued has as its

goal the production of a potent anti-serum against distemper. Efforts to do this at an earlier stage in the work were unsuccessful, but lately, owing to the greater knowledge of immunity against the disease which has been obtained, a renewal of these attempts has led to more promising results. If a powerful anti-serum could be made, it would offer an alternative method of immunising dogs, namely the simultaneous injection of anti-serum and living virus: the former would prevent the animal from having more than a mild and brief attack of fever, while the latter would confer a lasting resistance. The possible advantage of this method is that it would involve only one injection and might thus prove more manageable in practice than the method of vaccination described in detail in the appended report. Further, a really powerful anti-serum might provide a useful curative treatment for dogs already suffering from distemper, if administered in the early days of the disease.

It may be repeated, however, that for the prosecution of these additional endeavours it is necessary that the investigators should be freed from the handicap now imposed by requests for vaccine from those who have found it useful in the course of experimental trials, and from others who have learnt of the results.

Whatever fortune may attend further work, whether in the near future or in other hands at a more distant date, the Research Committee are confident that the work already done has resulted in a substantial measure of practical success, upon which the investigators are greatly to be congratulated. The Committee hope that appropriate commercial development will shortly bring the benefits of this work to the dog-owning public and will result in a great diminution of the ravages of distemper among dogs.

CHARLES J. MARTIN (*Chairman*).
J. B. BUXTON.
S. R. DOUGLAS.
F. HOBDAY.
A. J. SEWELL.
November 15th, 1928. A. L. THOMSON (*Secretary*).

A REPORT UPON THE CAUSE AND PREVENTION OF DOG DISTEMPER.

By P. P. LAIDLAW, B.Ch., F.R.S., and
G. W. DUNKIN, M.R.C.V.S., D.V.H.

(From the Farm Laboratories of the National Institute for Medical Research, Mill Hill, Middlesex, England.)

Historical Introduction.

DOG-DISTEMPER is justly regarded as the most serious disease which threatens the well-being of the canine population of this country. It pays no respect to race or breed, but attacks the high-born and the low-bred animal alike. At times it may cause a comparatively trivial illness of a transient nature, and at others infection is followed by a serious and prolonged illness with a high mortality rate. Cases which ultimately recover from the more severe forms of the malady frequently show some pronounced disability which places the animal at a serious disadvantage with its fellows.

Distemper has apparently existed for very many years. Laosson (1882) in his review of the history of the disease attributes the first record to Aristotle, but in this instance, as is also the case with many of the other early records, the description of the disease is so scanty that identification with distemper must remain uncertain. In this country distemper was certainly present early in the nineteenth century for it attracted the attention of Jenner (1809) who considered that the disease had existed for more than 50 years previously, but had been confused with rabies. He gives a masterly description of the disease as observed amongst fox-hounds, draws comparisons between this and the infectious fevers of man and describes a detailed routine for the disinfection of kennels, which, however, gave disappointing results in practice. Delabere Blaine (1817) considers the disease was unknown in England about 1700 though very common in his day. Distemper was then, and had been for years, rampant on the Continent of Europe, but at this time it was believed that cat-distemper was identical with dog-distemper. Laosson (1882) and Karajewski (1882) adduced experimental evidence in favour of this view, with the result that confusion persists, in certain quarters, to the present day.

Distemper appears to have been confused with jaundice (yellows) and also with rabies. Numerous examples of records of the disease might be quoted, but summed up they show that distemper was present in the canine population of most countries of the world for very many

years and from time to time in different places there might occur a sudden increase in virulence of the disease with disastrous results for the dogs in question.

The recognition of the importance of bacteria as causes of disease towards the close of the nineteenth century, naturally led to the search for an organism which could be shown to be the causal agent of dog-distemper, and from time to time, new organisms were isolated and claims put forward on their behalf. Galli-Valerio in 1896 claimed to have secured cultures of the responsible organism. Copeman (1900) isolated a small bacillus which he considered was the infecting agent and prepared a vaccine for the prevention of the disease. In 1905 von Wunschheim isolated a small bacillus which he regarded as of the first importance. An entirely different view was put forward by Carré (1905), who claimed that it was possible to transmit dog-distemper by means of filtrates of infective material and that the filters might be so fine that no known visible organism could pass through them. In other words Carré was convinced that the infecting agent was so small as to be invisible under the modern microscope. Kregenow (1906) in a series of carefully conducted experiments entirely failed to confirm Carré's results, and Carré's conclusions were not generally accepted. Lignières (1906), who had previously regarded an organism isolated by himself as the true infective agent, repeated some of Carré's filtration experiments and abandoned his original conclusions and accepted those of Carré.

In 1911 from two independent sources there was announced the isolation of an organism from cases of dog distemper. This organism is now named *Bacillus bronchisepticus*, and is probably identical with that previously isolated by Copeman in 1900. M'Gowan (1911) was able to isolate this organism from the majority of distemper dogs and also found it in other species of animals including man. Ferry (1911, 1912, 1912-13) found this organism in the great majority of distemper cases when they were examined in the earlier stages of the disease, and frequently found it in pure culture in the respiratory tract. Torrey and Rahe (1913) also showed that this organism was present in many cases of distemper and might be secured in pure culture. The evidence in favour of this organism playing an important part in the disease is thus weighty for all these workers adduced evidence that the bacillus, when recently isolated, was pathogenic for dogs. They claimed, indeed, that the disease produced by the bacillus was genuine dog-distemper, and if their conclusions were correct, it would seem that Carré's view was wrong. Ferry (1914) showed that *B. bronchisepticus* might pass certain bacterial filters in small numbers, but the fundamental divergence between the two schools remained for Carré claimed

XUM

that the disease might be transmitted to young puppies by filtrates from which no bacterial growth could be secured, and *B. bronchisepticus* is an organism which is readily grown on ordinary laboratory culture media ; the other school maintained that this easily-cultivated organism was the primary cause of the disease.

At the time the Scientific Committee of the Field Distemper Council commenced its work, this divergence in view regarding the ætiology of the disease was considered of the highest importance, and a decision between the two opposing views was a necessary preliminary to much further work. Critical examination of the claims for *B. bronchisepticus* being the causal agent showed that the production of typical disease by cultures of this organism was not convincing. The difficulty of proof was recognised by the discoverers of the organism. The previous research workers never knew for certain that the experimental dogs used for their tests were susceptible to the disease, or if they had, at some time, suffered a mild attack of distemper, recovered therefrom and become immune. An experiment in which no typical result followed inoculation of the bacillus could be explained away by supposing that the animal was immune from the first, leaving only the successes to be considered. Again, the disease is so highly infectious and the mode of spread was so little understood, that it was very difficult to guard against accidental infections during the course of crucial experiments. These considerations were recognised by M'Gowan, who stated that accurate experimental work in infecting dogs was almost impossible. He performed a few experiments with his cultures, but does not consider them free from error. Ferry, and Torrey and Rahe, also saw the difficulties, but conducted experiments under the best conditions they could secure. These four workers considered that their experiments, though not conclusive, indicated that *B. bronchisepticus* was the causal organism. Similarly critical examination of the claims for protection of dogs against the disease by means of cultures of this bacillus, vaccines, etc., shows that the ordinary dog is of small value for such experiments. If some of the dogs are immune when they come up for experiment, some degree of success is sure to follow *any* vaccination method and until really large numbers are dealt with the net result may be quite misleading. It was thus abundantly clear that for accurate research a supply of dogs of known susceptibility was essential. The only way to secure this was to breed dogs specially for the purpose under conditions which would guarantee that the experimental animal had never come in contact with distemper infection. It was decided that the only method which would ensure this was : to breed the dogs inside a ring fence in the strictest possible isolation ; to remove the

parents from inside the ring as soon as practicable ; and do everything possible to prevent infection from gaining access to the susceptible stock. It was recognised that this decision involved considerable outlay, considerable expense in upkeep, and serious delay in experimental work with dogs. But experience has amply justified those responsible for the decision, for there is now available a supply of dogs of known susceptibility which the research workers consider an inestimable advantage for all experimental work and especially in all protection experiments. Without this supply of dogs, the work would have been very much more difficult and the interpretation of many experiments would have remained doubtful. Another advantage of the special supply of dogs was the fact that all animals were in first-class health and condition at the time they came under experiment, with the result that it was possible to study distemper in its simplest form uncomplicated by secondary infections.

It may be noted here that the maintenance of this clean stock of dogs for four years without distemper appearing shows that the disease does not arise spontaneously, and it is very probable that all cases of distemper are due to transference of infection from one animal to another.

The Compound.

The arrangements for the breeding of the susceptible dogs were as follows : A piece of ground on the farm was selected some hundreds of yards removed from all buildings and was completely enclosed by corrugated iron fencing sunk three feet into the ground and extending six feet above the surface. Inside the enclosure, towards one end of the compound, 16 kennels were erected and each kennel was provided with an appropriate enclosed run open at the top. Towards the other end of the compound, a small bungalow was built to accommodate two kennel maids, who were expected to live inside the compound, isolated with the dogs. At one corner of the iron fencing forming the wall of the compound, a small building was made, and this formed the sole means of entrance or exit from the enclosure. This building was divided into three compartments. Entering the building from without the compound, the first compartment forms a disrobing room, the second a bathroom, and the third a dressing room where sterile clothing is available. From the third compartment a door opens into the interior of the compound. The arrangement will be made clear by reference to the ground plan of the compound and its buildings. (This has been illustrated in *The Field*.—Ed. V.J.)

On every occasion of entry into the isolated area, the routine of disrobing, bath, donning sterile clothing, is carried out. The number of persons allowed to enter is strictly limited. At one other position

in the wall of the compound there is a second small building, which consists of two compartments. The first forms a small storehouse for food, etc.; the second is fitted as a sterilizing room and contains a large copper and an autoclave. A small hatchway is the only means of communication between this building and the interior of the compound. All food for the dogs is boiled or autoclaved before being passed through the hatchway, with the exception of a ration of cod-liver oil for the younger animals. All blankets, etc., for the dogs are autoclaved, and as far as it is practicable, everything entering the compound is sterilized.

It will be observed that the precautions taken to prevent infection spreading to the interior of the compound are very elaborate, but it was felt that no risks should be taken with a disease which is known to be so extremely infectious. After the first introduction of dogs into the compound, everything went well for some weeks. But distemper occurred, and the entire stock of dogs was removed and a fresh start made. It may be pointed out that the occurrence of distemper in the compound *now* would cause some 12 or 18 months' interruption in the work, for it would be necessary to start all over again and build up a new stock of susceptible dogs.

For the past four years the isolation compound has been working smoothly owing to the loyalty and care of those entrusted with the administration of the routine, and their attention to the disinfecting ritual which is insisted upon. It is clear that some small oversight or carelessness in disinfection or sterilization might admit infection to the compound with disastrous results, and Mr. G. Gamage's services here have been invaluable. It must be remembered further that the life of comparative isolation led by the kennel maids within the compound must have been tedious and at times irksome. Miss Smith and Miss Hyslop followed by Miss Gray and Miss Reason, have been unremitting in their care, and owing to their expert attendance the dogs and puppies have flourished.

As soon as practicable the original stock introduced into the compound was withdrawn, and the longer the work is carried on the more remote is the contact of this stock of dogs with distemper. There is no evidence that the stock is increasing in sensitivity to the disease, but it is of enormous assistance to work with dogs of known susceptibility, and this has been possible for the last four years.

The Arrangements for Experiments with Dogs.

With such an infectious disease as distemper it was evidently necessary to try and exclude all possibility of accidental infection occurring in the animals under experiment. The dog hospital,

XUM

was built originally for experiments on dogs. It is a fly-proof structure divided into two symmetrical portions by a central *post-mortem* room. Each of these portions consists of a series of cubicles, completely separated from each other, arranged about a central hall which contains a large tank of disinfectant. The building is heated and the walls and roof are lined with "Uralite" and the joints sealed as completely as possible. Entrance to either half of the building is only possible through a short corridor, the floor of which is sunk and contains constantly three inches of disinfectant solution. Every person entering the building wears rubber boots to thigh or knee, and a rubber-covered overcoat which overlaps the boots. On entry into the building, boots, coats and hands are washed with disinfectant.

After every visit to a cubicle containing an animal, whether showing symptoms or apparently normal, the rubber armour is washed down with disinfectant once more. The floors of the central halls are thus kept wet with disinfectant all the time work is in progress, and any infective material settling on coats or floors is rapidly sterilized. No two cubicles are opened at one and the same time.

At the outset of the work, this method appeared to be satisfactory, but it was discovered that when most of the cubicles were filled with experimental dogs, infection would spread within the building to healthy control animals in spite of the rigid antiseptic precautions. Work with ferrets showed that it was not possible to limit the spread of infection in a small closed space, and another plan of experiment had to be devised. The experimental house is now used as a dog hospital for special cases and for work with ferrets.

It was believed that the infection was due to contamination of the air enclosed in the building, and a series of kennels were constructed and scattered about the grounds around the laboratory buildings. Each kennel had a small run attached, was surrounded by fencing and wire netting and was separated from its nearest neighbour by a distance of 15 or 20 yards. The attendants wear the rubber equipment previously described, and are washed down with disinfectant before and after visiting any single kennel. Working in this way the free dilution by the external air appears to have prevented air-borne infection from occurring, and it has proved possible to keep a susceptible dog for months in one kennel while experiments were carried on in the adjacent kennels. As far as can be ascertained there are only two instances of accidental infection during the time this system has been in use, so that on the whole it may be said that the method has proved satisfactory.

After kennel and run had been inhabited by infected animals they required disinfection, and for this purpose a thorough scrub and wash

down with a disinfectant, such as one per cent. Lysol, was found to be all that was required. The infecting agent is readily destroyed and there is no evidence of infection persisting in the kennels after such treatment. A disinfected kennel may be used the following day with safety.

Experimental Distemper in the Dog.

The experience of workers in the field shows that dog-distemper is a disease of variable severity with symptoms of protean character. The divergence in symptoms is so great that some observers distinguish several types of the disease; and it was possible, when the work began, that there were really several distinct diseases grouped under the term distemper. It may be said at once that the experimental work indicates that dog distemper is a single entity, and that there is no evidence of several diseases masquerading under one name. A dog which is immune to one strain is immune to strains from other sources.

Everyone is agreed that the variable symptoms are due, in part at any rate, to mixed infections and that the secondary infections are responsible for much in the sum total of the disease. Broncho-pneumonia for example, is met with in distemper cases, but it is not an essential part of the distemper picture; many dogs pass through distemper without any sign or symptom of pneumonia. When pneumonia occurs it is due to the invasion of damaged lung tissue by a secondary infection. The naturally occurring disease is spread by contact between diseased and healthy dogs, and there is thus an excellent chance of the secondary infection being passed on at the same time. In kennels with packs of hounds or in dog hospitals where numbers of animals are in close relationship, the chances of the spread of secondary infections are greatly increased. It thus comes about that distemper as seen by the veterinary surgeon is frequently a complex.

Under experimental conditions the position is very different. Here infection is thrust upon a perfectly healthy dog by a method which excludes the secondary infecting agent with the result that distemper develops in its simplest form and, as a rule, runs an uncomplicated course.

Experimental distemper may be defined in brief as follows:— Dog distemper is an acute infectious fever characterised by an incubation period of four days, a coryza at the onset of the disease, an unusual temperature curve, severe gastro-intestinal disturbance and a variable set of symptoms due to inflammation in the respiratory tract. In a proportion of cases nerve symptoms, due to an encephalitis, may develop.

The incubation period is remarkably constant. It is occasionally

as short as three days and may in exceptional cases be prolonged to six days, but in the great majority of instances it is four days.

The onset of the disease is sharply defined by fever and a watery discharge from the eyes and nose. The discharge is frequently trivial, even in very severe cases, but it may be profuse. Within 24 hours the discharge may become faintly purulent, and the conjunctivæ acutely congested. Crusts of half-dried cells collect at the angles of the eyelids, and a purulent discharge may persist throughout the illness.

The temperature rises abruptly at the commencement of the illness and may reach 105° F., or even more, within 24 hours. After one or two days it subsides to near the normal level of 101·4° F.; but it soon rises again. The second rise is usually slower than the first and more prolonged. Its duration is exceedingly variable and may be as short as 48 hours in the mild cases, or as long as three weeks in the more severe cases.

At the onset of the disease the dog usually vomits and refuses food. With the fall of temperature appetite returns for a time, to diminish once more as the secondary fever develops. In practically every case there is diarrhœa and in the secondary febrile period; this may be profuse. The motions are slimy, may contain streaks of blood, and have an offensive and somewhat characteristic odour. The diarrhœa may persist for some days after the remission of the fever. The poor appetite coupled with the diarrhœa interferes with the nutrition and the animal wastes rapidly.

Symptoms from the respiratory system are usually slight. A slight cough is not uncommon in the period of secondary fever, but definite bronchitis or bronchopneumonia does not occur. At the same time, there is nearly always some evidence of inflammation in the respiratory passages during life or at autopsy.

Involvement of the nervous system may take place early or late in the disease and is very variable in occurrence. The earliest symptom is a sudden attack of semi-consciousness with vigorous chewing movements, accompanied by the secretion of thick saliva which exudes from the angles of the jaws. The fit may pass off after a few seconds or persist for a minute, after which the dog appears to be perfectly conscious once more. Fits of this type may occur at irregular intervals, but as a rule they come more severe and merge into attacks of epileptiform convulsions. Muscular spasms and twitches may be observed in those cases which develop nerve symptoms late in the disease, and these in turn may become exaggerated and lead to convulsions. Whenever fits were observed the affected animal was destroyed with chloroform, so that there is no information as to the late results in the nerve type of case.

XUM

The following brief notes and temperature charts of cases will illustrate the variability of the experimental disease. Chart I shows the temperature record of a case of acute uncomplicated distemper

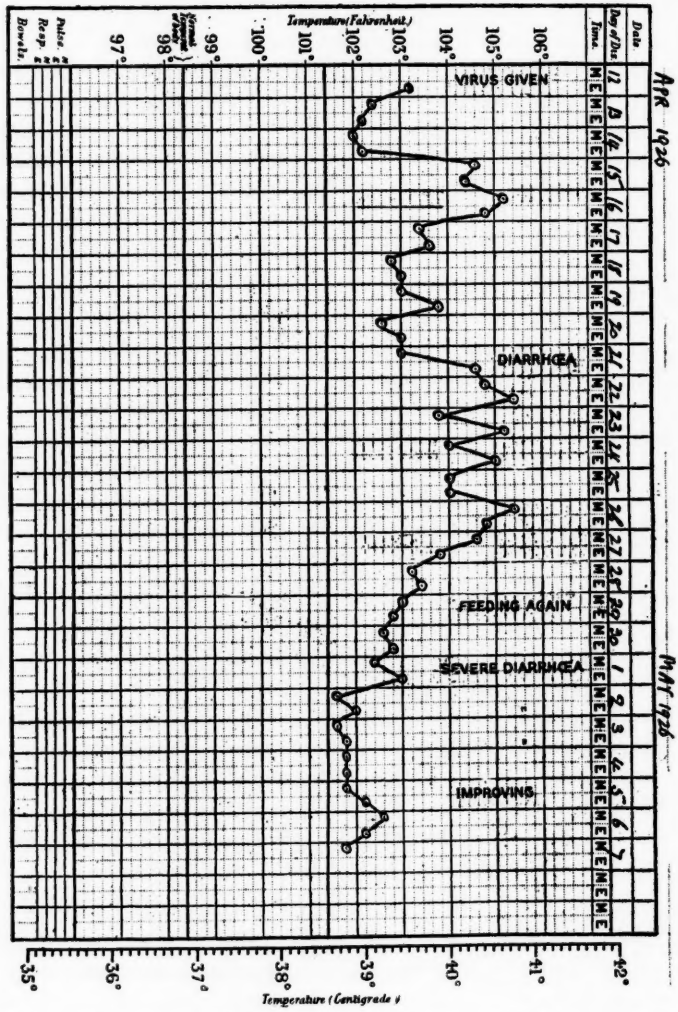

CHART I.

with respiratory symptoms. The diphasic temperature curve is typical. In the second febrile period there was severe diarrhœa, cough was persistent, there was no sign of pneumonia although this

complication was feared on the twelfth day, when the patient was transferred to the dog hospital. Appetite was very poor and the dog wasted rapidly, but recovery eventually occurred.

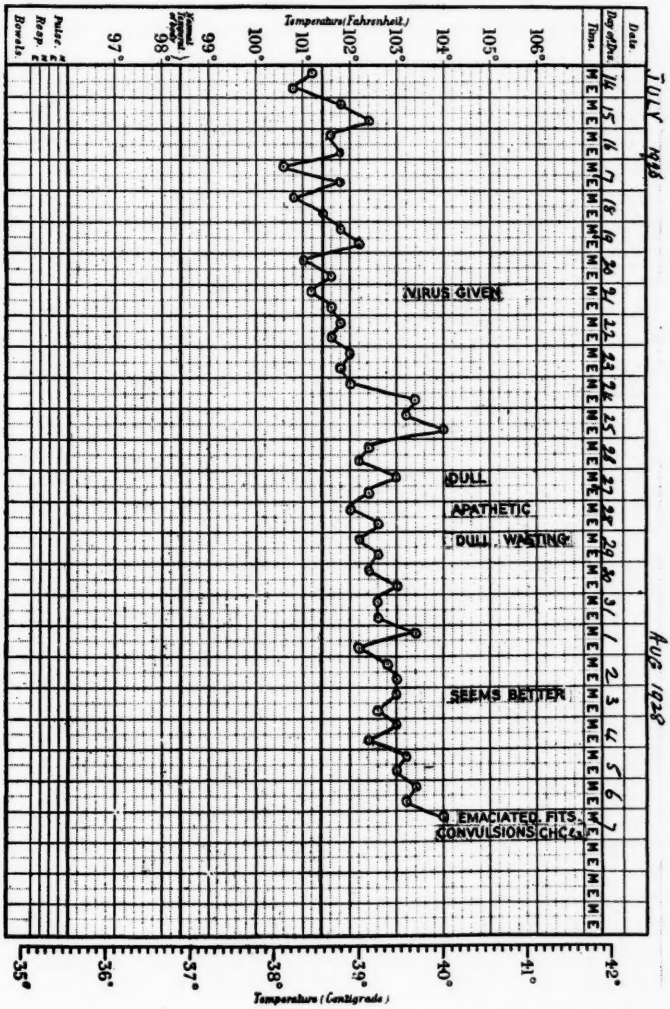

CHART II.

Chart II illustrates another type of distemper attack where the fever does not seem to be so severe, but the dog was always much worse than the temperature indicated. Fourteen days after the

beginning of the second febrile period fits developed and the animal was destroyed with chloroform. Cases of this kind are not uncommon, and the termination with fits may occur much earlier or much later. The relatively low temperature in a hard hit animal is of grave import.

Chart III illustrates a very mild distemper attack. There was comparatively trivial bodily disturbance, and the dog did not lose condition. A subsequent injection of a large dose of another, virulent, strain of virus produced no effect of any kind. This illustrates immunity in a dog and also the fact that a dog immune to one strain is immune to others.

Chart IV is shown to illustrate an overwhelming infection. Here the response begins in a typical manner, but at the end of a week collapse ensues and the dog dies with a subnormal temperature. This type of response is more frequent in young puppies.

Chart V shows another unusual result which may occur in very young puppies. Here there is still noticeable the diphasic temperature response, but the puppy did not seem seriously ill at any stage. Suddenly fits supervened.

The response in very young puppies is frequently atypical, and only a few experiments were done with puppies about two months old.

Experience of distemper under experimental conditions shows that it is a disease of very variable severity. The variation is partly attributable to differences in susceptibility in dogs, but it is clear that different strains of virus possess different degrees of virulence. Taking all cases together, it may be said that experimental distemper is a disease with a comparatively low mortality rate. There are cases in which the infection overwhelms the patient such as that illustrated in Chart IV, but these are unusual and occur for the most part in quite young puppies. Cases which show signs of infection in the nervous system are always serious, but they again only account for a proportion of the whole. For the rest, though the disease may be acute and the animal hard hit for a time, the prognosis is good. This finding is, at first sight, at variance with the experience of workers in the field, but is readily explained by the absence of secondary infections under the best experimental conditions. Dog-distemper may be regarded as an acute infectious fever, comparable in many respects with influenza or measles in man, a disease which by itself will produce a severe fever and serious bodily disturbance, but is rarely fatal, and yet a disease which may light up a latent infection or enable secondary infections of various kinds to gain a foothold on damaged tissue.

Experimental work also shows the extremely infectious nature of distemper in the early stages of the disease. At the onset of the disease before symptoms are manifest, the distemper dog is a source

of danger to its fellows. The nasal discharge and the circulating blood are uniformly infective at the early stages of the disease and uncertain in the later stages. There is evidence that infection may

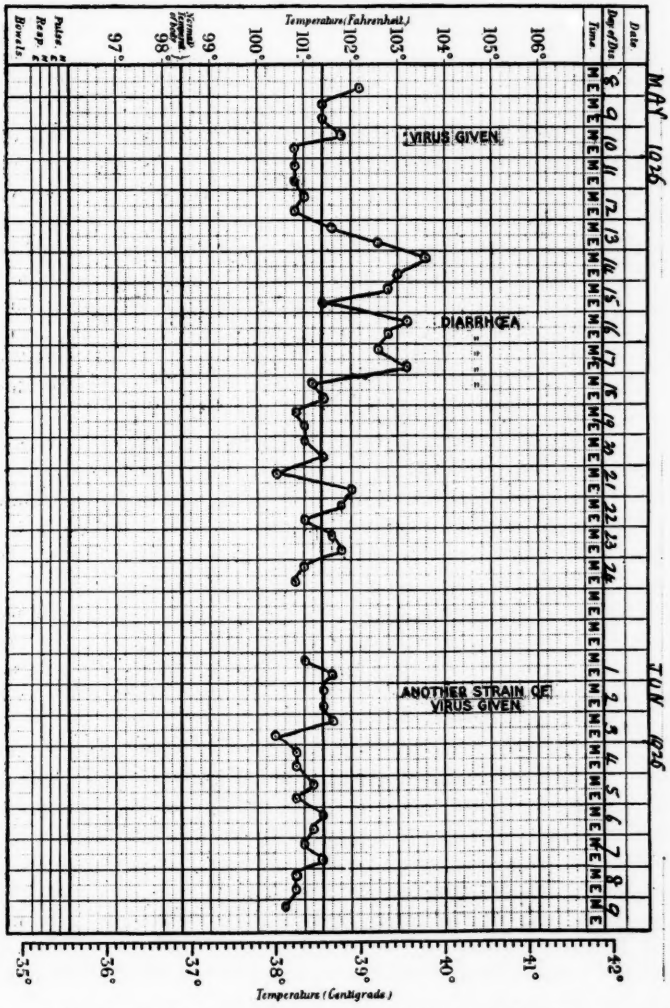

CHART III

spread for short distances through the air in a confined space, and that actual contact between animals is not necessary for the transference of infection from one dog to another. It is probable that in

these cases the infection enters by the respiratory tract, and corresponding with this, it is quite easy to infect a dog by the insufflation of a small quantity of virus into the nasal passages. No evidence of an ectoparasite acting as a vector of infection has been discovered.

Vesico-pustules, which have been and in certain quarters still are regarded as a diagnostic sign of distemper appear to be only indirectly connected with the disease. They may occur in susceptible animals without any other symptom, and after recovery from the eruption, the dogs are fully sensitive to small doses of distemper virus, and the resultant disease runs a typical and unmodified course. Dunkin (1926). In many cases of experimental distemper, vesico-pustules are never seen throughout the whole course of the disease. The contents of the pustule will not infect, nor will they induce protection in a susceptible animal. Laosson (1882). It seems clear, therefore, that the eruption is due to some cause other than distemper, and when it develops in a case of this disease, it must be due to some secondary infective agent. The occurrence of pustules may suggest distemper and draw attention to other symptoms of greater significance, but by themselves they are insufficient to justify a diagnosis of dog-distemper.

As distemper is a disease of very variable severity, in the milder cases it may be very difficult to diagnose it with certainty. Cases occur in which a bi-daily temperature record is almost the only guide to a correct diagnosis, and temperature charts should be of the greatest value to the clinician in all doubtful cases ; isolated records are, on the other hand, of much less value.

During the first febrile period the dog may show very few clinical symptoms, and yet at this time his secretions and excretions, as also his blood, are all very infective for susceptible animals. The isolation of animals from their fellows at the earliest stage of the disease would probably do much to stop the spread of infection.

As stated above, uncomplicated distemper is not a very fatal disease for healthy animals, if the cases which develop nerve symptoms are excluded. Efforts should be made to keep cases of distemper separate from each other as it is exceedingly probable that the crowding of dogs together is largely responsible for the spread of secondary infections. These secondary infections may be the determining cause of death. For example, broncho-pneumonia developing in a dog already depressed and weakened by the distemper infection is always serious and may lead to a fatal outcome though the distemper infection by itself might have been overcome with ease.

Close contact between susceptible animals during a distemper outbreak leads inevitably to the rapid passage of the disease from dog to dog. Under these conditions it is to be expected that the virulence of the disease will increase and, though there is no experi-

mental proof of this rise in virulence, it is so probable on general grounds that ample spacing for animals must be strongly recommended to dog owners.

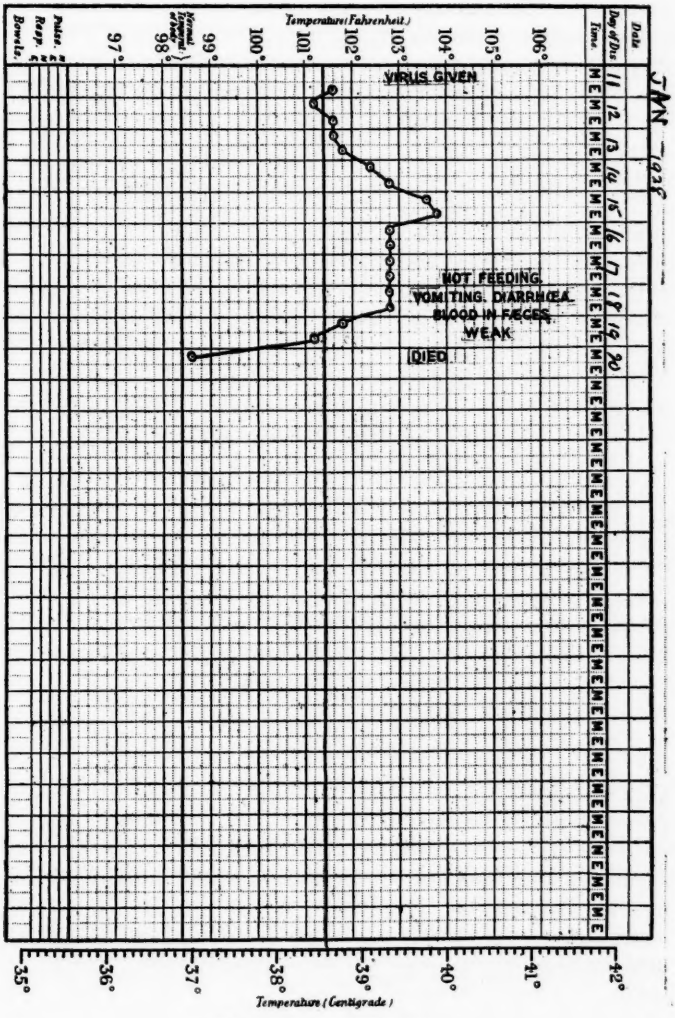

CHART IV.

Distemper in Ferrets.

When the investigation was being planned, it was felt to be highly desirable to be able to employ some animal other than the dog for

certain phases of the work. If possible the alternative animal should be small and capable of being maintained in rigorous confinement. Unfortunately dog-distemper is not a disease which can be communicated to the ordinary laboratory animals. Rabbits, guinea-pigs and white rats are resistant to infection. The records of distemper in wolves, wild dogs, lynxes and racoons, in captivity, did not help, Fox (1923). The distemper in the foxes in the silver fox farms, studied by Green (1925) is probably dog-distemper as Laosson (1882) found no difficulty in transmitting dog-distemper to two captive foxes. Distemper in cats was believed by many to be the same as distemper in the dog. There was even some experimental evidence in favour of this view, Laosson (1882), Krajewski (1882), but a number of experiments were made by us, and all gave completely negative results. The hedgehog was used by Sanfelice (1915) and was reported by him to be susceptible when injected intracerebrally. In the only experiment tried, a hedgehog proved resistant to a massive dose of virus administered subcutaneously. Ferrets were reputed to be very susceptible to dog-distemper, and these were tested and found to be admirably adapted for experimental work. It may be noted in passing that the weasel and the stoat have also been found to be susceptible animals.

In several respects the ferret is a peculiarly suitable animal for the experimental study of dog-distemper. First, it is exceedingly susceptible to infection. Secondly, the disease is nearly always fatal. On account of these two facts, it is very unusual to find a resistant animal in a batch of ferrets purchased in the open market. Thirdly, the ferret will thrive in the most rigorous confinement, which is a very important point when studying such an infectious disease as distemper. Fourthly, the ferret breeds readily and quickly, if it is kept under good conditions and well fed.

The ferret has been employed extensively throughout the whole investigation, and it is not too much to say that such success as has been achieved is largely due to work with ferrets. It is needless to state that all crucial experiments have been confirmed on dogs, but the use of the ferret allowed a great deal more work to be carried out and at the commencement of the work when the specially bred dogs were not available, the ferrets proved invaluable.

The majority of the ferrets used for the investigation were specially bred for the purpose, but purchased animals have also been used freely. The ferrets are bred in a special hut about 40 yards distant from the nearest distemper area. The hut is fly proof, and warmed in winter time. The attendants never come in contact with distemper cases and are not allowed to keep dogs of their own. Visits to the hut are discouraged. The ferrets are fed on raw horse meat and milk

with an occasional ration of bread. Two litters of young are obtained each year and occasionally three. The average number in the litter is nine.

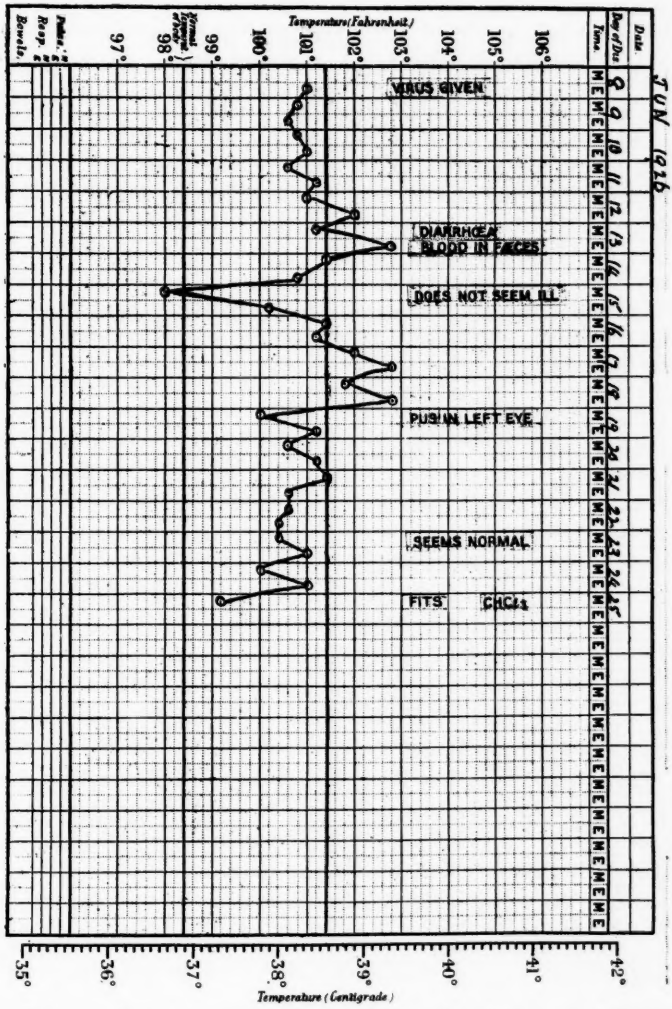

CHART V.

For experimental purposes the ferret is placed in a special cage made of sheet zinc, which is similar to that designed by Prof. Topley for the study of epizootics in mice. This type of cage allows of

observation of the animal for prolonged periods without handling it, and thus eliminates one possibility of unconscious transference of infection. The Topley cage containing the ferret is placed in a cubicle in the experimental house previously described, and thus a second barrier is raised against the spread of infection. The attendants wear the rubber armour, which is washed down with disinfectant between visits to different cubicles.

Working in the above manner it has proved easy to limit infection to a single cubicle, but it has not been possible to prevent the spread of infection within a cubicle. A control (uninoculated) ferret may be kept for weeks in one cubicle, while infected ferrets are tended in the adjacent compartments and infection does not spread to the control animal. On the other hand, if there be two ferrets in Topley cages inside one cubicle, one of which is infected and the other uninoculated, infection of the control animal occurs. The most plausible explanation for this result, which has been obtained on several occasions, is the air-borne infection occurs. This view is in harmony with the fact that infection may pass from dog to ferret without any actual contact occurring. It is sufficient to bring ferret and a distemper dog near together, for a time, in a confined space and the ferret will acquire the disease. Again, this explanation is in harmony with the results which have already been reported in the case of dogs.

It is not surprising, in view of the spread described above, to note that contact between sick and normal animals for a brief time leads to a spread of the disease or that the introduction of a clean ferret into a cage from which a sick ferret has been removed results in infection of the sound animal. Minute quantities of blood or tissue from a sick ferret will almost invariably cause disease in a susceptible animal if injected subcutaneously.

In the case of the ferret there is usually an incubation period of about 10 days, during which time the infected ferret appears to be quite normal. When very large doses of virus are given, and especially when the strain of virus is a potent one, the incubation period may be shortened to six or seven days. When small doses are given, the incubation period may be prolonged.

The onset of the disease is shown by watery discharge from the eyes and nose. Within 24 hours the discharge becomes faintly purulent and the eyelids frequently become puffy. The chin is reddened and soon minute vesicles appear at the junction of the naked skin of the lip with the fur. The feet become swollen, the pads red, and occasionally the skin on the lower half of the abdomen and inner aspect of the thighs becomes reddened. On the third day the vesicles on the chin become small pustules and the ferret remains curled up in a corner.

refusing all food. Improvement is quite unusual, and the ferret becomes gradually weaker and is often moribund on the fifth or sixth day. Occasionally the progress of the disease is slower, and an animal may remain in a sick state for more than a week, but ultimately the ferret dies from inanition, bronchopneumonia, or convulsions. Cases which appear to be recovering frequently relapse or succumb to acute nerve symptoms. The clinical picture is thus fairly characteristic and as there are not many mild cases of distemper in this species, the ferret is a very useful test animal to employ in those cases where the diagnosis in dogs remains doubtful.

Ferrets which did happen to recover from one attack of distemper proved to be resistant to infection, not only by the strain of virus which caused the original disease, but also to all other strains of distemper which were obtainable.

The Nature of the Infecting Agent in Dog Distemper.

Quite early in this report it was pointed out that there were two divergent views regarding the ætiology of dog distemper. The one supported by M'Gowan, Ferry, Torrey and Rahe taught that the disease was due to *B. bronchisepticus*, a recognisable bacillus with definite morphology and cultural characteristics ; the other, supported by Carré, considered that the infective agent was an ultramicroscopic organism.

Experimental work with ferrets and dogs soon showed that the view of Carré was probably the correct one. As has been pointed out, it is exceedingly easy to transmit the disease to a healthy dog or ferret by injecting a minute amount of blood or emulsion of tissue taken from a diseased animal, and yet it has always proved to be impossible to secure cultures of an organism resembling *B. bronchisepticus* from such material. In the great majority of cultural experiments, the infecting blood and tissue proved to be sterile. In this connection it may be mentioned that the advocates for a bacterial origin of the disease admit that they were nearly always unable to secure cultures of bacteria from the circulating blood, so that the new results are in agreement with theirs in this respect, but it must be added that blood, if collected early in the disease, is one of the most certain agents that can be employed for the transmission of infection.

Direct confirmation of Carré's filtration experiments was not so easy and all the earlier experiments gave negative results. For a time the experience was similar to that of Kregenow, who failed in every instance to secure infective filtrates. Ultimately it was found possible to filter the infecting principle through standard bacterial filters with uniformly successful results. Infective filtrates were

secured when employing Pasteur Chamberland L2 filters, Mandler filters, and membrane filters of known porosity. All these filters are known to retain nearly all visible bacteria, and it was further demonstrated that the filters actually employed would hold back bacteria and yet allow the infecting principle to pass. Filtration of biological fluids and mixtures through filters of the type commonly employed by bacteriologists is exceedingly complex and many factors are involved, each of which may alter the result of a given experiment. The analysis of the factors involved in this problem has engaged the attention of Mr. Elford, who is working under the supervision of Mr. Barnard. It may be mentioned that quite recently Mr. Elford has succeeded in filtering distemper virus through membrane filters of standard porosity, and the data available indicate that the organism causing distemper is of the same order of size as the organism causing pleuropneumonia of cattle.

Throughout all the experimental work efforts have been made to secure cultures of the infecting agent, but in every instance failure has resulted. In no experiment has there been found any evidence of multiplication of the virus. In some experiments the virus persisted for a short time, but in every case it ultimately died. Subcultures were never found to be infective for healthy animals. This experience is in harmony with the view expressed above regarding the ætiology of the disease, for it is the experience of nearly all laboratory workers that with the single exception of pleuropneumonia of cattle filterable viruses cannot be cultivated on any ordinary culture medium. Efforts are still being made to secure cultures of the distemper virus as this is regarded as essential to complete success, but it is now doubtful if any satisfactory result can be achieved.

The results of the work so far recorded confirm the view propounded by Carré, viz. that dog distemper in its simplest form is an acute infectious fever caused by a filterable virus or ultramicroscopic organism. This fever lowers the body resistance to other infecting agents and as a result complicated cases of distemper are common. In field work and in crowded kennels complications are the rule.

The Immunization of Ferrets.

A ferret, just as appears to be the case with a dog, which has recovered from one attack of distemper is immune to further attacks of the disease. This immunity is solid and lasts for a long time, probably for life, and forms a very striking contrast to the susceptibility and low resistance of the normal animal. Experiments were therefore undertaken to try and discover some method of bringing about the resistant state without causing active disease. It was considered

probable that any method which proved successful in the case of the ferret would also prove efficacious, with minor modifications, in the case of the dog.

Experiments have shown that it is possible to induce a considerable degree of resistance in the ferret by the administration of vaccines. This resistance may be consolidated and rendered durable by the injection of a dose of appropriate living virus. The vaccines employed differ in detail according to the method of manufacture, but they all consist essentially of virus which has been inactivated (killed) in some way. The treatment of the virus must not be too drastic or the efficacy of the product diminishes. The vaccine causes no significant bodily disturbance, but renders the ferret, after a short time interval, resistant to the living virus which was used in the manufacture of the vaccine. The animal which has received both vaccine and virus is solidly immune.

The vaccines are thus similar to the bacterial vaccines which are employed extensively to-day (typhoid vaccine). There is, however, a very important difference. Bacterial vaccines made from artificial cultures of bacteria are carefully controlled and even counted if it is desired. As has been explained, the distemper organism in spite of long continued effort, has not yet been cultivated on artificial media, and therefore the best raw material for the manufacture of vaccine is not available. Experiment showed that certain tissues of distemper ferrets, taken at the height of the disease, contained a large amount of the infecting agent, and further that the amount might be adequate to allow of the pounded tissue being converted into an efficient vaccine by several different methods of treatment. The method is far from ideal and is lacking in precision. For example, the virus content of the raw material cannot be measured with accuracy, and thus the potency of the final product is variable and indefinite. In spite of the drawbacks the method has proved to be exceedingly useful in actual practice, and the results were a great encouragement to explore similar channels for the immunization of dogs.

The spleens from sick ferrets may be converted into efficient vaccines in several different ways. These have been described by us in a recent publication (1928a) and need not be referred to in detail as ultimately choice was made of one method which gave excellent results not only in the case of the ferret but also in the case of the dog.

The Manufacture of Vaccine for Ferrets.

Ferrets suffering from acute distemper are killed by an overdose of chloroform on the fourth or fifth day of illness when they are usually *in extremis*. The carcass is dipped in two per cent. Lysol

and pinned out. The spleens are removed with sterile instruments, using strict aseptic precautions. The spleens are weighed, pounded in a sterile mortar and rubbed up into a smooth mass as quickly as possible. Sufficient saline is added to yield a 20 per cent. suspension of spleen pulp, and after brief stirring the contents of the mortar are transferred to a sterile bottle containing glass beads. The bottle is shaken vigorously in a machine until all the fragments seem to be broken up. The contents of the bottle are then filtered through a double thickness of sterile butter muslin, into a sterile bottle. All shreds of tissue are thus removed and discarded. A small quantity of the filtrate is removed for a potency test. Sufficient strong formaldehyde solution is added to the main bulk to yield a final concentration of 0·1 per cent. after which the mixture is shaken and transferred to the cold store. After four days the formolised spleen suspension is invariably non-infective for ferrets, and sterility tests are made, both for ærobic and anærobic bacteria. If the product proves to be sterile, as is usually the case, it may be used as a vaccine without any further treatment. Owing to the presence of a small amount of formaldehyde, however, vaccines of this kind are irritant when injected subcutaneously. A non-irritant product can be made by adding sufficient ammonia solution to give a faintly alkaline reaction. In practice ammonia is added until a reaction of pH 8·0 to pH 8·2 is secured, and thus all free formaldehyde is converted into urotropin and the final product is devoid of irritant properties.

For the potency test referred to above, the 20 per cent. suspension of spleen pulp is diluted freely and doses corresponding to 1/10,000 grm. and 1/100,000 grm. of spleen are injected into two ferrets. Both animals should sicken with distemper within ten days. If they do not do so it is clear that the virus content of the material which was converted into vaccine was low and the resultant vaccine will probably prove to be inferior. Owing to the long incubation period of distemper in the ferret it is necessary to assume that the material will yield a good vaccine and finish the preparation of the vaccine at one sitting. It is not advisable to keep the ferret spleens whilst the potency of these organs is being determined, as during the wait of ten or more days considerable deterioration will occur in the virus content of the tissue.

Experience of upwards of 40 different batches of vaccine prepared in this way shows conclusively that it is not difficult to secure a product which is fairly uniform and usually quite efficient, while if due care be taken and the concentration of formaldehyde recommended be employed there should be no difficulty in securing a sterile product.

The complete immunization of ferrets is achieved as follows :—

Small areas of skin in the selected animals are shaved and sterilized by the application of tincture of iodine. Two cubic centimetres of vaccine are injected through the sterile area into the subcutaneous tissues by means of a syringe and fairly large hypodermic needle. The animal is put aside for two weeks. At the end of this time a quarter of a cubic centimetre of living virus (approximately a hundred fatal doses for an unvaccinated animal) is injected either into the skin or subcutaneously. The strain of virus should be the same as that employed in the manufacture of the vaccine. No symptoms should follow the administration of the vaccine or the virus, and a fortnight after the last injection the ferret should be immune to all strains of distemper virus, whether secured from ferrets or dogs.

With this technique it proved possible to immunize about 90 per cent. of ferrets at will, and the immunity was shown to last for months. Immunized ferrets have been placed with interested landowners who have promised to work them as usual and to report on the after history of the animals. In some instances reports have been received stating that the immunized ferrets have withstood infection, but naturally in many instances exposure to infection has not yet occurred. In one instance four immunized ferrets were placed with eight others and worked as usual. In the course of time distemper appeared in the ferretry. The four immune animals survived without showing any symptom of the disease, the eight untreated animals all died. Up to date no adverse report has been received regarding these immunized animals.

The vaccine made by the method described has been shown to keep for some months without serious deterioration, and it was found that organs other than spleens might yield vaccines with similar properties. On the whole, however, the spleen gave the best and the most uniform product.

In concluding the consideration of the immunization of ferrets, it may be pointed out, even at the cost of reiteration, that crude distemper virus (distemper ferret tissues) may be inactivated with formaldehyde, and that virus so treated forms an efficient vaccine. One dose of this vaccine renders a ferret resistant to infection by some hundreds of fatal doses of the same strain of virus as was used for the manufacture of the vaccine. A ferret which has received both vaccine and virus becomes immune to all strains of distemper virus.

Vaccination alone (the injection of formolized material only) is inadequate to ensure a solid and lasting immunity. Experiments showed that the resistance following vaccination is gradually lost. After three to five months some of the ferrets which were tested with living virus showed symptoms but ultimately recovered. In other

experiments, the protection was so poor at the end of a year that one half of the experimental animals died after the injection of living virus.

The Immunization of Dogs.

There is good evidence that one attack of distemper in a dog, followed by recovery, results in a solid immunity which lasts for life. Put in another way, a dog but rarely has more than one attack of distemper. It is true that there are instances in which distemper has been diagnosed more than once in the same dog, but it is probable that in the majority of these instances there has been some mistake in the diagnosis. Mistakes in diagnosis are inevitable in the case of a disease which varies so much in severity and in which complications are so common and so prominent that the underlying infection is not suspected, or if it is suspected, cannot be definitely recognised. In some few instances it is possible that particular dogs have had multiple attacks of distemper, just as there are human beings who have been subject to more than one attack of measles, but it appears to be the general rule that one attack of distemper confers lifelong immunity, just as is the rule with measles. This striking immunity has led every research worker to attempt the immunization of dogs, whenever he was convinced that he had discovered the cause of the disease. It is only reasonable to suppose that if the actual agent which produces distemper were discovered, it should be possible to induce immunity by vaccines made from this agent. However that may be, it is clear that the majority of those who have claimed that a given organism was the cause of distemper have supported their claim by accounts of protection conferred on dogs through the use of vaccines, sera, etc., made from their supposedly causal organism.

Copeman (1900) maintained that vaccines of his organism were of value to preventing disease. Phisalix and Lignières, who independently isolated what appears to have been the same organism, also considered that the favourable results attributed by them to vaccination indicated that their bacillus was the true infecting agent. Phisalix vaccine was investigated by a committee in this country, and the report was not favourable. *B. bronchisepticus* isolated independently by M'Gowan, Ferry, Torrey and Rahe, has been converted into vaccines, and these have been very extensively used in the treatment and prevention of distemper. The good results which were reported did lend support to the view that the causal organism had been discovered, but Hardenbergh (1926), in a recent analysis of a series of cases, failed to find any good evidence that vaccines of this organism conferred protection against the disease.

It may be fairly said that none of the vaccines made from visible

bacteria have been successful in preventing distemper in a long series of cases. They have not stood the test of time, though at the outset the results seemed favourable. It is very probable that the research workers were misled through unwittingly carrying out experiments on dogs which had previously had distemper in a mild form and were, therefore, immune from the start. In this connection it must again be emphasised that a specially bred dog is an inestimable boon to the research worker, for work of this type. Even so, the disappointments of the past serve as a warning to the investigator to be cautious in interpreting all protective experiments.

As has been indicated previously, the evidence secured from the study of the experimental disease shows that the visible bacteria which have been isolated from time to time are not the cause of the acute infectious fever which is the foundation of all cases of true distemper. The visible bacteria are to be regarded as secondary invaders, and as such, play a subsidiary part. Their importance varies from case to case, and it remains quite possible that bacterial vaccines may be favourable in diminishing or limiting the complications which are all too common in this disease.

Putting on one side the protection experiments with visible bacteria, there remain a few records of attempts at immunization by other means. Bryce (1882) collected blood from a distemper dog, boiled it and added carbolic acid. The resultant product was injected into two puppies, and the result was considered favourable, but the work does not appear to have continued. Puntoni (1923 and 1924) propagated distemper virus from dog to dog by intracerebral injection and found that the brains of such dogs were rich in infective material, and yet free from ordinary bacteria. The infecting agent in emulsions of such brains might be inactivated by formalin, and the resultant product would form an efficient vaccine. His work was hampered and at times interrupted by his failure to secure susceptible animals as and when they were required. Towards the end of 1927 Lebailly (1927) claimed that it was possible to make efficient vaccines from the spleens of dogs suffering from distemper. The account of his experiments is brief and certain important details are lacking, but he also seems to have secured some measure of success.

No exact repetition of Puntoni's work was attempted, as this would have involved the passage of distemper virus intracerebrally, with the result that there would have developed symptoms of distemper encephalitis, and it did not seem probable that this particular form of encephalitis could have been recognised with certainty. It was more probable that errors would have arisen. The work of Lewy and Kantorowicz (1923), Lewy, Fraenkel and Kantorowicz (1925),

Lewy, Lewy and Kuttner (1926), showed quite clearly that the study of distemper by intracerebral passage was beset with special difficulties which make the interpretation of the results uncertain. Puntoni's results have been tested indirectly by the manufacture of vaccines from the brains of dogs with the acute nerve form of distemper, and it is clear that vaccines so prepared may be of considerable value. Lebailly's results were tested, as his experiments were very similar to those which gave good results in the case of the ferrets. There is no doubt that it is possible to prepare vaccines along the lines followed by this worker, but the method he followed is capable of improvement in several important particulars.

Ferret Vaccine for Dogs.

The vaccines which proved to be so valuable in the protection of ferrets were tested on dogs, and it was found that a single dose of such a product was inadequate to protect a dog against a dose of living virus. The size of the dose was increased, and the results did not appear to be much better. Multiple doses were then tested, and it was found that if three doses were given at intervals of a week, a resistant state might be established in every case. The degree of resistance varied slightly from animal to animal, but the vaccinated dogs always showed a very mild response to the injection of living virus, whereas the control (unvaccinated) dogs developed an unmodified disease.

Five separate experiments were carried out to determine the value of triple vaccination with vaccine prepared from ferret spleens. Twenty dogs in all were vaccinated three times, and 15 others were employed as controls. The controls were kept in the kennels alongside the vaccinated animals throughout the whole experimental period. One or sometimes two weeks after the last dose of vaccine had been given the control and the vaccinated animals were injected with living virus, and the responses in the dogs were noted. Bi-daily temperature records were kept of all animals throughout the whole experiment. The 20 vaccinated animals all did well, and only five of them had any considerable degree of fever, which, however, was of quite short duration. In none of this series was there any untoward symptom throughout the mild illness, which would probably not have been recognised as distemper by an impartial observer. The majority of the 15 controls had typical acute distemper attacks, and the diagnosis was usually obvious. In the control group there were, however, only two fatal cases, and there were three examples of very mild disease. It seemed clear that a very considerable degree of protection could be secured by the three doses of vaccine. It was further established

that the dogs which had received living virus were solidly immune, for large doses of living virus could be injected subsequently and no disturbance followed. Again, it appeared that any strain of distemper virus could be injected with impunity. The work was extended to privately-owned hounds and dogs, the owners of which were willing to try and secure immunity even though the immunization technique could not be guaranteed to be free from risk. The results of the field work will be considered later. Here it may be noted that the results seemed good, but there were no adequate controls.

Consideration of the method shows that it is far from ideal, and though of considerable theoretical interest, it is not of great practical utility. In the first place the amount of vaccine which can be obtained from a small animal like the ferret is not great, and the time occupied in the whole process of immunization is considerable, lasting, as it must, for more than a month. Moreover, it was disappointing to find that a vaccine, which in a single dose protected ferrets completely, did not give absolute protection to a dog after three injections at intervals of a week.

The Manufacture of Vaccine for Dogs.

The results claimed by Puntoni and later by Lebailly seemed to be superior to those which were secured by the use of ferret vaccines, and it was considered possible that the difference might be due to the fact that both these workers employed dog tissues in the manufacture of their vaccines. Efforts had been made early in the work to secure vaccines from dog tissue, but all the experiments were disappointing. Renewed efforts which included the examination of dog tissues harvested at different stages of the disease, led to the production of very efficient vaccines from the distemper dog. The details of this work have just been published (1928b), and reference must be made to the original paper for all details by those interested.

The vaccines were made in the manner that has already been described for ferret material. It was found that abdominal lymph glands, spleen, liver and brain, might all be made into efficient vaccines on some occasions and not at others. A review of the successes and the failures indicated that the first prerequisite for the manufacture of good vaccine is a rich supply of virus in the organs from which it is made. When the virus content of the tissue selected from the distemper dog was shown to be high (minute doses proving infective for ferrets) the vaccine proved to be efficient. When the virus content of the tissue was low the vaccine made from it usually proved to be inferior. For example, the brain in the average case of distemper does not contain much virus, and if it is employed for the manufacture

of vaccine, the resultant product is worthless. The brain in the acute nerve type of distemper sometimes has a high virus content, and can then be converted into good vaccine by the ordinary method. The

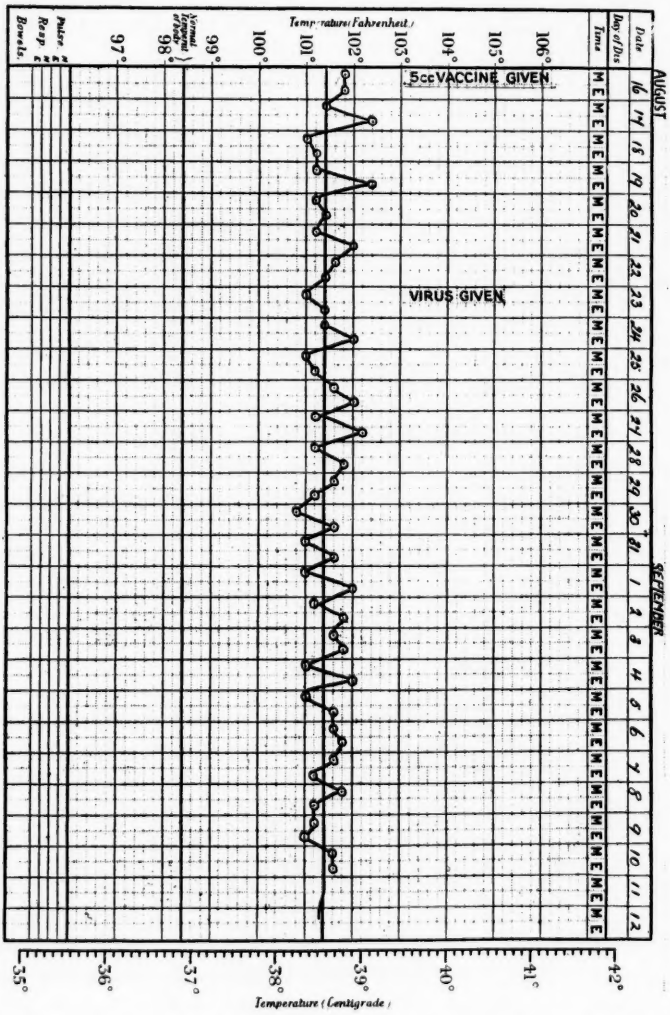

CHART VI.

abdominal lymph glands and spleens gave almost uniformly good results when the tissues were collected between the 7th and 18th days following infection. Spleens collected at the time recommended by

Lebailly—the height of the first febrile reaction—did not give such good results. The liver was variable, but with this organ again it was found that if it contained much virus, the vaccine made from it was

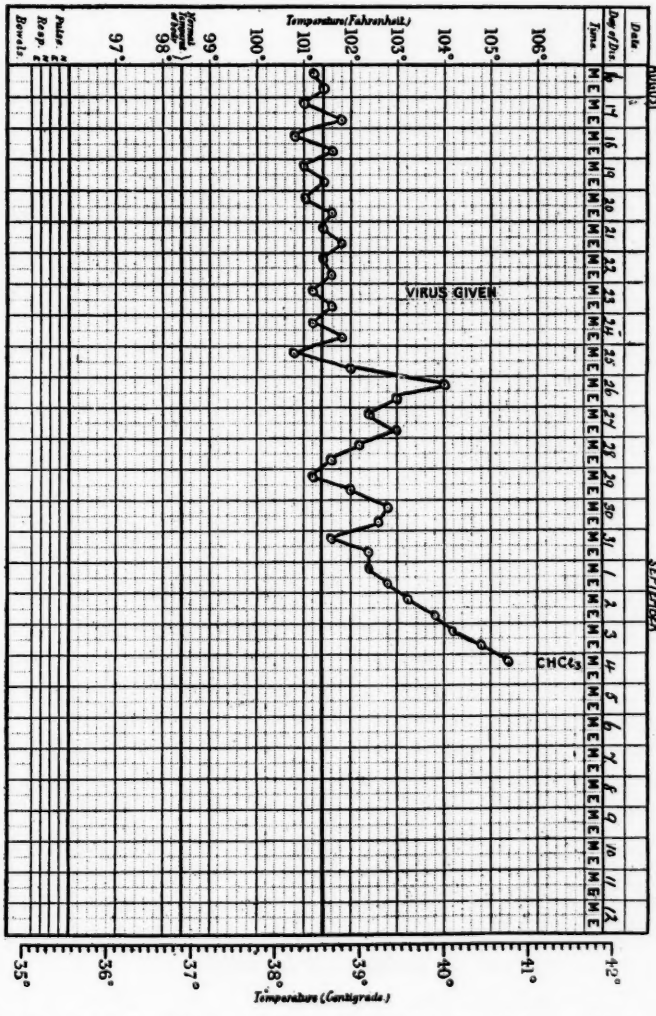

CHART VII.

usually of good quality, and if the liver did not contain much virus, the resultant vaccine proved to be inferior. It does not seem possible to choose an optimum time for the collection of these tissues as the

difference in response in different dogs is so great, but it is clearly advisable only to collect tissues from dogs which are hard hit by the disease, and preferably at the time when they appear to be at their worst. Experience of a number of successes and failures allows one to form a good idea as to which tissue should be included in the batch of vaccine in any given case. On several occasions it has proved possible to work up liver, spleen, lymph glands and brain together and secure more than a litre of vaccine from one distemper animal. There is still, however, a great deal of work necessary in order to define the conditions for the manufacture of vaccine in quantity, and of uniformly good quality.

The results with a good batch of vaccine made from distemper dog tissue are really most remarkable. A single dose of five cubic centimetres of vaccine, administered subcutaneously, will induce such a degree of resistance in the recipient, in one week, that injection of a large dose of virulent virus produces very little effect. There may be some slight fever for a day or two accompanied by alimentary disturbance, but the dog remains cheery, active and takes its ordinary ration with gusto. The control animal has an acute fever, often vomits and refuses all food, has severe diarrhœa, wastes rapidly, and is nearly always dull and apathetic within four days of the onset of the disease. Charts VI and VII illustrate the responses in a vaccinated and a control animal respectively. The vaccine was made from a mixture of tissues from a distemper dog. The difference in the temperature records is striking, and the difference in symptoms was equally obvious. Chart VIII illustrates another vaccinated animal's response to a potent strain of virus, and it will be seen there is a little fever for two days. Another animal of the same litter was vaccinated at the same time, with an equal dose of vaccine, and gave no response whatever to the living virus. Chart II is reproduced again, as this represents the response in the control animal. In this case the fever is not so violent as in the previous control animal (illustrated on Chart VII), but the dog became rapidly worse and ultimately developed fits which necessitated its destruction. Many more cases in illustration might be given, but they all show that it is possible to secure from distemper dogs a vaccine which will confer almost complete protection after a single dose of 5 cc. administered hypodermically.

A Satisfactory Immunity.

Dogs which have been immunized by vaccines followed by living virus prove to be solidly immune. They resist large doses, not only of one strain, but of all strains of distemper. They may be placed in contact with acute cases of the naturally occurring disease and do

not become infected. They have further been shown to be immune to virus given intracerebrally, so that it would seem that the nervous system partakes in the general immunity. As far as can be determined,

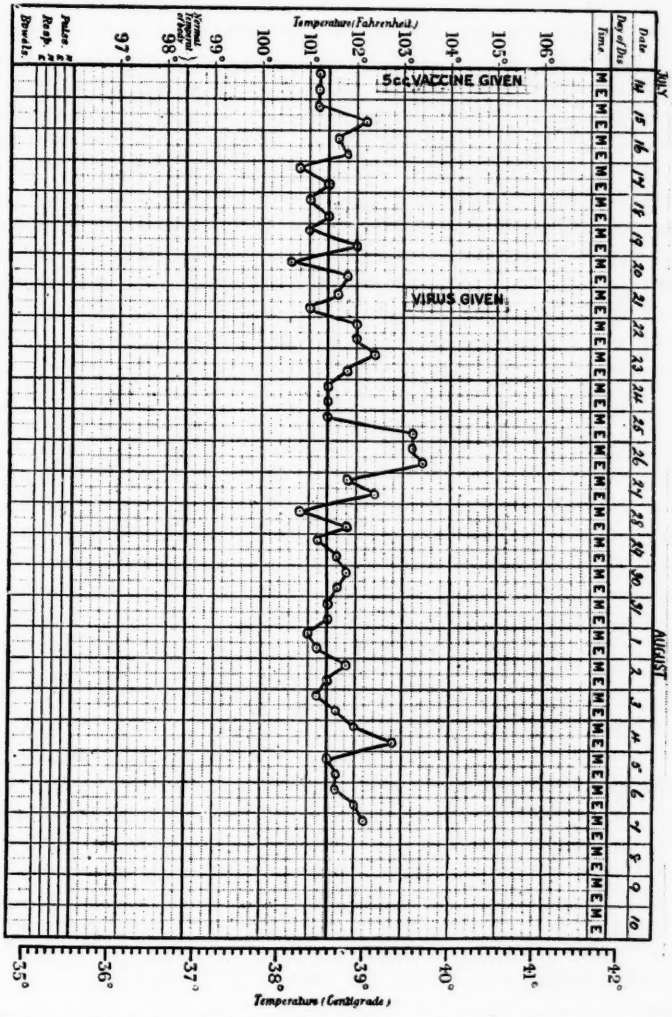

CHART VIII.

the immunity is long-lasting. Certain dogs were placed with persons interested in the work, and they promised to report if ever distemper symptoms developed. No report of this nature has been received.

The results with this technique seemed so good that work with privately-owned hounds and dogs was undertaken on a larger scale, and the results will be found summarised towards the end of this report. It should be emphasised that the complete immunization process includes the administration of living virus as a final measure. For test of resistance induced by vaccines a potent strain of virus is used, but for field work a weak strain, which appears to have become attenuated for dogs through oft-repeated ferret passage, is employed. Further, it should be noted that the vaccinated dog which develops a mild fever following the injection of living virus does not appear to be a source of danger to susceptible animals. It is quite likely that on occasions where the response to the vaccine was poor, and where consequently the modified distemper attack following the living virus injection was severe, infection *might* spread, but experiments have shown that it is legitimate to carry out the whole of the immunization process in contact with susceptible animals. In no instance did infection pass from the treated animal to the susceptible companion.

From what has been recorded regarding the two types of vaccine, it will be seen that a single dose of vaccine made from ferret tissue is sufficient to protect a ferret against the living virus, but three doses of this product are required to induce a resistant state in a dog. On the other hand, a single dose of vaccine made from dog tissue may render a dog irresponsive to living virus. The value of dog vaccine for ferrets thus became of interest, and it was found in a series of experiments to be nearly worthless. Three doses of dog vaccine, of proven quality for dogs, given at intervals of a week, did not appear to evoke any resistance in ferrets. The vaccinated animals seemed just as susceptible as the controls.

Thus, ferret vaccine is good for ferrets and relatively poor for dogs; dog vaccine is good for dogs and bad for ferrets. The fact that the homologous vaccine is superior to the heterologous, in the case of dog distemper, is not only of practical importance, but also of considerable theoretical interest, and it would probably repay further study.

The results in this special case are not directly transferable to other diseases due to filterable viruses, but, if borne in mind, they should prevent undue optimism regarding complex vaccines of the kind under discussion. These may prove to be efficient with one species of animal, but it does not follow that they will be as efficient with other species.

Preventive Serum.

In the case of diseases in which recovery is followed by a solid and durable immunity, it is frequently possible to demonstrate pro-

tective substances in the blood of the immune animal and to increase the amount of the circulating protective substances by repeated injection of the noxious agent (hyperimmunization). If such substances are produced in reasonably large amount, it is sometimes feasible to collect the blood from an immune or hyperimmune animal, separate the serum and use this serum for immunizing susceptible stock. In the case of Rinderpest, for example, the injection of serum along with virus produces a mild type of the disease and, on recovery from this, the animal is immune. The amount of serum and the dose of virus have naturally to be nicely proportioned.

It was considered possible at the commencement of the work that dog distemper might belong to this class of disease, and that it might be possible to secure a serum with valuable protective properties. As was reported previously, all the earlier experiments gave negative results, and it was stated that the immunity of the recovered dog, or ferret, was not due to circulating antibodies, but to the resistance of his tissues. The serum of recovered animals did not appear to delay the onset, or modify the severity, of an attack of distemper. At this stage of the investigation serum from hyperimmune dogs also did not give encouraging results, and this line of investigation was abandoned for a time.

Quite recently the matter has taken on an entirely new aspect, for it has been shown to be possible to secure a serum with valuable protective properties. This advance appears to be due to the fact that we now know how to secure material very rich in virus and the administration of this to immune animals leads to the appearance of antibodies in the blood. It appears to be necessary to inject some millions of infective doses, preferably more than once, into the recovered animal in order to secure a valuable serum, and the virus employed must be taken from the same species of animal as is used for the manufacture of the serum.

Little work has, so far, been carried out with the serum, as there has been considerable pressure on the staff and equipment in endeavouring to define the conditions for making distemper vaccines. It seemed better policy to consolidate that success before commencing intensive work in the new channel. It may be said, however, that the serum is sufficiently potent to prevent a small dose of virus causing disease. Dog serum, which is the only serum so far secured, will only work in dogs ; it does not prevent or seem to modify the disease in the ferret. It is impossible to assess the value of the new serum until much more information is available, but it should be possible, by grading the dose of virus and serum, to establish the immune state in a susceptible dog with very little bodily disturbance. It is

even possible that a serum-virus method may, in the end, prove superior to the vaccination-virus technique. It is possible that really potent serum might prevent disease after infection had occurred, but before symptoms developed (serum treatment in the incubation period of the disease). It is also possible (though it is felt to be improbable) that a potent serum might be of use in treating animals in which the disease was already established. Finally, it is highly desirable from the scientific standpoint that the mode of action of protective sera in the case of diseases due to filterable viruses should be studied in detail. At the present time, as the work of Andrewes (1928) shows, the way in which these sera prevent disease is ill-understood, and the older conception of their action must be reconsidered.

The Protection of Privately-Owned Hounds and Dogs.

The successful immunization of dogs under laboratory conditions led naturally to an extension of the work into the field in various parts of the country. Many dogs, of various breeds, have now been immunized by veterinary surgeons according to the technique described above and with material supplied from the Farm Laboratories. Altogether, 949 dogs comprising various breeds have been treated by 44 veterinary surgeons during the last two and a half years. The practices of these gentlemen are scattered over the British Isles in such widely-separated localities as Perth, Tiverton (Devon), Watford, Margate, Hereford, Manchester, Malton (Yorks), Co. Tyrone, etc.

Results Secured by the Vaccine.

It will be convenient to consider the results secured under two separate headings : 1. Foxhounds. 2. Dogs of other breeds.

1. Foxhounds.

From the information available it appeared that the most anxious time for masters is that which follows on the assembly of hounds into kennel from walk. In many instances distemper breaks out about this time and, partly owing to the overcrowding which frequently exists, the disease runs riot through the whole of the young entry. In view of this state of affairs, the practice recommended was to administer the vaccine while the hounds were still at walk and to inject the virus just after assembly. With this procedure hounds should have developed some degree of resistance, in response to the injection of vaccine, by the time they were assembled, and accidental infection in the kennels was of small moment because a final injection of living virus was always given to consolidate the immunity.

This procedure was sometimes difficult to follow. In some hunts the walks were so widely separated that it was thought to be impracticable to proceed along these lines, and in one case hounds were assembled before the injections commenced. The result was disastrous, for distemper broke out before the immunization was completed, and of the 10 couple in question five couple died. At the same kennel 11 couple were vaccinated at walk and given virus on assembly. They were housed with non-vaccinated hounds. Distemper broke out. One immunized hound died and 66 per cent. of the uninoculated hounds perished.

Three hundred and twenty-five couple of hounds belonging to 15 different packs have been treated. The number of inoculated hounds in each of these packs varied considerably, but it was usually small as the amount of vaccine available was not large. In all cases the vaccination was confined, for obvious reasons, to the young entry. Some disappointment has been caused among masters of foxhounds at the paucity of puppies it has been possible to inoculate, but clearly the extent of the field work has been limited by the supply of vaccine available. The shortage of vaccine, although unfortunate from the owner's point of view, has actually been of assistance to the investigation. Had there been unlimited supplies of vaccine and all, or most, of the susceptible hounds in any pack been immunized, the results would have been much more difficult to interpret owing to the absence of control animals. Untreated hounds of the same stock and age running with the immunes form an index for the incidence and severity of distemper in the kennels, and allow one to judge of the degree of protection afforded by the inoculation.

Both masters of foxhounds and veterinary surgeons have been most kind in supplying information regarding the condition of hounds during the inoculations, the occurrence of any outbreak of distemper in the packs, and the results in the immunized and untreated animals. It may fairly be said that the inoculations gave very little trouble, and there was only one case of a hound dying during, and possibly as a result of, the inoculations. In the great majority of instances the whole immunization was carried through without any anxiety. Some of the hounds were immunized more than two years ago, and others have been done quite recently. In some cases they are known to have been exposed to infection, and in others they have not yet come in contact with the disease, so that the degree of protection is not known in some instances. The records from certain packs are, however, so striking that hopes are raised regarding the whole. A few reports may be quoted :—

THE PUCKERIDGE.—In this pack 12 couple were inoculated in

February, 1928. In April of this year distemper broke out in the uninoculated hounds, but none of the treated hounds developed the disease. Thirty-five couple of uninoculated hounds contracted distemper and 11 couple died.

THE TIVERTON.—The master reports in a letter dated July 8th, 1928, as follows: "Of the young entry for 1927 and 1928 which had been inoculated, none had distemper. There was an outbreak of this disease in the kennels in December, 1927, among the two-year-old hounds, but none of the vaccinated hounds developed the disease. Four vaccinated hounds were sent to neighbouring kennels in which distemper was present, but none of them were ill."

THE WARWICKSHIRE.—Twenty-two couple of the young entry of this pack were inoculated in March, 1928. The master, replying to a questionnaire, has written as follows: "All the inoculated hounds have been exposed to distemper infection, but none has contracted the disease. Forty-five and a half couple of uninoculated hounds have developed distemper, and of these 24½ couple have died."

2. Dogs of Other Breeds.

Two hundred and ninety-eight dogs of various breeds have been dealt with, including the following: Labradors, wire-haired terriers, dachshunds, Cairn terriers, golden retrievers, spaniels, pointers, bull terriers, bulldog, whippet, toy spaniels, Dandie Dinmonts, Skye terriers, Shetland collie, Alsatian, retrievers, mastiff, Kerry blue, Keyshond, Aberdeen, etc. The inoculation of these dogs, including the administration of living virus, was carried through without serious trouble or anxiety in nearly every instance. One Dandie Dinmont died following, and probably as the result of, the administration of virus. A few dogs did not respond very well to the vaccine and had severe fevers following the virus, but these were of short duration.

The majority of the dogs in this group are well bred and frequently exhibited at shows where, as is well known, there is always an excellent chance of infection being acquired. The owners of these dogs agreed to report whenever an inoculated dog acquired distemper, and up to date no report of this nature has been received. On the other hand, information shows that the inoculated animals have withstood infection in certain cases. Four puppies belonging to a litter of wire-haired terriers were inoculated in May, 1928, and in a letter dated September 22nd, the owner states that two of these puppies have twice been in contact with other puppies which were suffering from distemper. No ill-effects followed this accidental exposure to infection from a case of severe distemper diagnosed and treated by a veterinary surgeon.

Fifty-two puppies in a well-known kennel of Dandie Dinmonts

have been inoculated during the past two years, and distemper has never been contracted by any of them, though they have appeared at dog shows. On two occasions the owner has purchased and introduced into her kennel an addition to her stock and both of these subsequently died of distemper.

The results of the field work, whether they concern foxhounds or other breeds of dogs, are most encouraging, and, coupled with the laboratory findings, they indicate that it is possible, or will be possible in the future, to immunize hounds and dogs at will. It is true that the inoculated animals have yet to stand the test of time, and it must be shown that the immunity does not deteriorate with age. In view of the fact that the final step in the immunization process consists in the administration of living virus, it is unlikely that the immunity will deteriorate. It is also desirable that larger numbers of hounds and dogs should be dealt with, but this is a matter of time and adequate supply of vaccine. So far as the results go they are most gratifying.

The Future.

It is hoped that the foregoing statement of the work which has been carried out under the auspices of the " Field " Distemper Fund will have given the reader some idea of the nature of the problem set before the research workers, some conception of the difficulties which were encountered and how they were met, and finally, the nature and the degree of progress that has been made.

There remains for consideration the aim and scope of future work. It is almost certain that the complete conquest of the distemper problem and the final subjugation of the disease is bound up with the successful cultivation of the virus apart from the living animal. In this direction no success has been forthcoming in spite of oft-repeated effort. It is desirable that renewed attempts should be made to overcome this outstanding difficulty. Baffled in this direction, it has yet proved possible to evolve a vaccination method which promises to do much to prevent the ravages of distemper in selected groups of animals. It is desirable that this vaccination method should be made as perfect as possible and as readily available as can be arranged, and efforts are being made with this object. Quite recently a protective serum has been secured, the value of which it is impossible to estimate at the present time. It may prove to be of practical utility or merely of academic interest. In either case it is desirable that it should be investigated to the limit of what is possible. These two lines of investigation have for their prime object the benefit of the majority of the canine population, but beyond this there is the value of the increased knowledge regarding an acute infectious fever, knowledge

which may suggest the correct method of study, or the best method of preventing or controlling infectious fevers injurious to other animals and to man.

PORTLAND (President),
On behalf of The "Field" Distemper Council.

REFERENCES.

Andrewes, C. H. (1928): "The Action of Immune Sera on Vaccinia and Virus III *in vitro*," *Journ. Path. and Bact. 31* (Part 4 in the press).

Aristotle: *Historia Animalium* Lib. VIII, cap. 22.

Blaine, Delabere (1817): "Canine Pathology" [etc.], 8vo, London [see p. 42].

Bryce (1882): "Inoculation as a Preventive of Distemper in Dogs," *The Veterinarian, 55*, p. 207.

Carré, E. (1905): "Sur la maladie des jeunes chiens," *C. R. Acad. des Sci. 140*, p. 689; "Sur la maladie des chiens," ibid, p. 1,489.

Carré, E. (1926): "La maladie des chiens," *Rev. gen. de méd. vét.*

Copeman, M. (1900): "The Micro-organism of Distemper in the Dog, and the Production of a Distemper Vaccine," *Proc. Roy. Soc. 67*, p. 459.

Dunkin, G. W. (1926): "Vesico-pustules and Distemper," *Vet. Rec. 6*, p. 193.

Dunkin, G. W., and Laidlaw, P. P. (1926): "Studies in Dog Distemper—I: Dog Distemper in the Ferret," *Journ. Comp. Path. and Ther. 39*, p. 201.

Dunkin, G. W., and Laidlaw, P. P. (1926): "Studies in Dog Distemper—II: Experimental Distemper in the Dog," ibid. p. 213.

Ferry, N. S. (1911): "Etiology of Canine Distemper," *Journ. of Inf. Dis. 8*, p. 399.

Ferry, N. S. (1912): "Bacillus bronchisepticus (bronchicanis) the Cause of Distemper in Dogs and a Similar Disease in other Animals," *Vet. Journ. 68*, p. 376.

Ferry, N. S. (1912-13): "Further Studies on the Bacillus bronchicanis, the Cause of Canine Distemper," *Amér. Vet. Rev. 41*, p. 77.

Fox, H. (1923): *Diseases of Captive Wild Mammals and Birds*, J. B. Lippincott Company, Philadelphia, London, Chicago [see p. 599].

Galli-Valerio, B. (1908): "Der gegenwartige Stand unserer Kentnisse von der Aetiologie der Hundestaupe," *II Abt. Ref. 41*, p. 563.

Green, R. G. (1925): "Distemper in the Silver Fox (Culpes vulpes)," *Proc. Soc. exper. Biol. and Med. 22*, p. 546.

Green, R. G. (1926): "Distemper in the Silver Fox (Culpes vulpes)," ibid *23*, p. 677.

Hardenbergh, J. G. (1925): "The Significance of Bacillus bronchisepticus in Cases of Canine Distemper," *Journ. Amer. Vet. Med. Ass. 68*, p. 309.

Jenner, E. (1809): "Observations on the Distemper in Dogs," *Med. Chir. Trans. 1*, p. 165.

Krajewski (1882): Original not available. Abstract in *Jahresbericht ueber die Leistungen auf dem Gebiet der veterinär Medicin. 2*, p. 45 (1883).

Kregenow, C. (1909): "Ueber die Filtration des Staupecontagiums," *Cent. f. Bakt. 1ste Abt. Orig. 50*, p. 326.

Laidlaw, P. P., and Dunkin, G. W. (1926): "Studies in Dog Distemper—III: The Nature of the Virus," *Journ. Comp. Path. and Therap. 39*, p. 222.

Laidlaw, P. P., and Dunkin, G. W. (1928): "Studies in Dog Distemper—IV: The Immunization of Ferrets against Dog Distemper, *Journ. Comp. Path. and Therap. 41*, p. 1.

Laidlaw, P. P., and Dunkin, G. W. (1928): "Studies in Dog Distemper—V: The Immunization of Dogs," ibid., p. 209.

Laosson, A. (1882): "Ueber die Geschichte und Contagiosität der Staupe," *Ing. Diss. Dorpat.*

Lebailly, C. (1927): "Vaccination préventive et spécifique des chiens contre la maladie du jeune age," *C. R. Acad. des Sci. 185*, p. 370.

Lewy, F. H., and Kantorowicz, R. (1923): "Neue parasitologische Befunde bei der nervösen Staupe der Hunde," *Arch. f. wiss. u. prakt. Tierhlk. 49*, p. 137.

Lewy, F. H., Fraenkel, E. und Kantorowicz, R. (1925) : " Encephalitis lethargica und Hundestaupe," *Klin. Wochschrft. 4*, p. 1,254.
Lewy, F. H., Fraenkel, E. und Kuttner, H. (1926) : " Encephalitis lethargica und spontane Tierencephalitis," *Klin. Wochschrft. 5*, p. 272.
Lewy, F. H., Lewy, F. M. und Kuttner, H. (1926) : " Encephalitis lethargica und spontane Tierencephalitis," ibid., p. 886.
Lignières, J. (1903) : " Sur le microbe de la maladie des chiens Pasteurellose canine," *C. R. Soc. Viol. 55*, p. 918.
Lignières, J. (1903) : " Sur la vaccination de la maladie des chiens," ibid., p. 921.
Lignières, J. (1906) : " Sur la maladie des chiens et le virus filtrant de Carré," *Bull. de la Soc. Cent. de Med. Vet. 83*, p. 622.
M'Gowan, J. P. (1911) : " Some Observations on a Laboratory Epidemic, Principally amongst Dogs and Cats, in which the Animals affected presented the Symptoms of the Disease called ' Distemper,' " *Journ. Path. and Bact. 15*, p. 372.
Phisalix, C. (1903) : " Observations à propos des deux notes précédentes de M. Lignières," *C. R. Soc. Biol. 55*, p. 921.
Puntoni, V. (1923) : " Saggio di vaccinazione anticimurrosa preventiva esiguita per mezzo del virus specifico," *An. d'Ig. 33*, p. 558.
Puntoni, V. (1924) : " Ancora sulla vaccinazione anticimurrosa per mezzo del virus specifico," *An. d'Ig. 34*, p. 406.
Report of a Committee (1904) formed to carry out experiments with the vaccine of Dr. Phisalix, *Journ. Comp. Path. and Therap. 17*, p. 274.
Sanfelice, F. (1915) : " Ueber die bei der Staupe vorkommenden Einschlusskörperchen," *Cent. f. Bact. 1ste Abt. Orig. 76*, p. 495.
Torrey, J. C., and Rahe, A. H. (1913) : " Studies in Canine Distemper," *Journ. Med. Res. 27*, p. 291.

THE CLINICAL RESULTS OBTAINED WITH DISTEMPER INOCULIN.

A Foreword.

By S. S. BILLINGTON, M.B., B.S., F.R.C.S.,
Leamington Spa.

BOTH in fairness to the inoculin, and in the interests of obtaining information on the distemper problem, I think a brief outline of the method of production during the last five years should be given.

As previously mentioned, my object was to grow the filter passer from the bacterium. I wished to obtain confirmatory clinical evidence that I had caught the correct raw material to work with, and with this object in view, the first editions of the therapeutic article were very carefully prepared. The results were so uniformly excellent in various parts of England and Scotland, that a few months sufficed to supply the clinical evidence sought.

The remedy was still produced, primarily, with the object of watching for the appearance of fresh strains of the organism ; but when it went off, it was found to be due to a reversion of the organism to the bacillus bronchisepticus stage.

It soon became apparent that the important part was not the specific antigenic protein, but something that the specific part carried.

By carefully checking the biochemical differences, I have been able to determine what this constituent is.

The varying clinical results have been due to this varying chemical factor, at times varied purposely, and at times because the correct therapeutic stage was not available when the inoculin was asked for. For the object in view, it was just as important to know which stage was more or less useless, as it was to know which was the effective therapeutic agent.

After a five years' interlude as regards concentrating on the technique of the preparation of the inoculin, I have come back to it with the biochemical information obtained during that period.

Two important points emerge from the indefinite distemper problem :—

1. A filter passer is the causal organism.
2. The bacillus bronchisepticus is not the cause, but a distemper immune serum contains antibodies for the bac. bronchisepticus.

The therapeutic article therefore, plus the filter passer, should produce bronchisepticus antibodies.

In the globulin coated stage of the organism, mobilisation of the globulin in a nascent carbon dioxide surrounding at room temperature, results in the disappearance of the bacillus, with the appearance, of what could be used for purposes of morphological demonstration as typical filter passers.

The correct inoculin dissolved in normal serum, and incubated with an emulsion of these tiny bodies, results in the production of an anti-bronchisepticus serum.

With the above information at my disposal I have no doubt that I can repeat and standardise the inoculin of five years ago, which, I believe, cured 97 per cent. of cases treated by one veterinary surgeon, and I know that another of my veterinary friends hardly lost a dog for nearly a year, when it suddenly went off.

Remarks on Prophylaxis.

I am frequently asked as to whether I have prepared a preventive vaccine, but I ceased to look in that direction for a preventive some years ago.

From the practical standpoint, dogs can be divided into three groups :—

1. Those that are more or less naturally immune.
2. Those that contract the infection, but make more or less uninterrupted recoveries.
3. Those that die unless provided with some specific help.

It is the third group that we are concerned with, and there is

obviously something absent which is present in the first group, and partially present or latent in the second group.

There is every reason to suppose that the immunity of group one is due to the presence of a biochemical entity, kept there by an efficient endocrine regulation. If this is the explanation, one would be surprised if the introduction of an attenuated virus into a group three dog produced a permanent immunity. In a group two dog, after an attack of the disease, one would expect the sluggish resistance to have been stimulated to leave a permanent immunity. In a group three dog, that would have died, but which had been helped over the crisis, one would not be surprised if a percentage failed to retain an immunity.

The preventive vaccine produced by the Commission will put the above considerations to the test. My investigation is a spasmodic affair carried on in spare moments ; but unless there is any unforeseen check, I shall have published a complete description of the various stages of the distemper organism, long before the lapse of necessary time to test out a preventive.

If it is found that the attenuated virus does confer a permanent immunity, it will be a simple laboratory performance to supply the virus in any desired stage of attenuation, at a very low cost, and without the necessity of destroying dogs for its production.

TUBERCULOSIS IMMUNITY.

By NATHAN RAW, C.M.G., M.D.,
London.

THE immunization of animals against tuberculosis is a problem of great magnitude and complexity, and a great many scientific workers are at present looking for a solution. It is estimated by competent authorities that at the present time there are in the British Isles about 1,000,000 dairy cows infected with tubercle, and that about 5 per cent. of them have tuberculosis of the udder.

The fact that the milk of a whole herd may be mixed before delivery may render the whole yield dangerous to children.

Several thousands of children are infected every year by tuberculous milk with truly terrible results. Almost all children and animals are born free of tubercle, and if they are not exposed to infection, they will never develop the disease. It is obviously impossible to eradicate tuberculosis from cattle by wholesale slaughter or any other means, as the cost would be prohibitive and the cattle could not be spared, so that we must direct our energies to the prevention of infection, and that can only be done effectively by rendering the young animals immune to infection.

For the last 25 years I have been working in the laboratory and have inoculated many hundreds of animals in an endeavour to find a vaccine to produce immunity. It is impossible to *completely* immunize an animal against tuberculosis, but it is possible to confer a relative immunity which is quite sufficient to protect it against the ordinary infection it may meet with in its ordinary life.

The vaccine which I use is prepared from dead cultures of human bacilli which have become attenuated through many years of continuous sub-cultures, and which are a virulent and non-tuberculogenic. In other words, they are incapable of producing tuberculosis in an animal. The method of inoculation or vaccination of a newly-born calf is as follows. The calf must be separated from its mother at birth and fed on boiled milk or milk from a healthy cow.

The first dose of vaccine is given hypodermically on the third day, and the second dose on the 14th day, under the skin of the abdomen. The calf is then protected and can mix in the herd.

Young cattle with a negative reaction to tuberculin can be treated in the same way.

Over 2,500 calves and young cattle have been treated by competent veterinary surgeons during the last four years, and the results up to the present are most encouraging. The duration of immunity is uncertain, but it is at least 18 months to two years, and probably more, but the process can be repeated if necessary, and is advisable.

The method is harmless, and can never in any circumstances produce tuberculosis, as the vaccine is prepared from dead cultures, on the same principle as vaccination against typhoid and para-typhoid with dead cultures of typhoid bacilli.

LAMB DYSENTERY PROPHYLAXIS IN 1928.

By T. DALLING, J. H. MASON and W. S. GORDON

Langley Court, Beckenham, Kent.

We have already recorded in brief some of the results of the use of vaccine and serum in the prevention of lamb dysentery during the 1928 lambing season.[1] A fuller account of the season's work can now be given.

Inoculation of Ewes.

In past years the vaccines used for ewe inoculation have consisted of a toxin of the lamb dysentery anaerobe neutralised by its specific anti-toxin, and with or without the addition of a killed saline

suspension of strains of *B. coli* isolated from lambs affected with lamb dysentery. The use of such vaccines has been followed by good results.[2] [3] [4]. Many thousands of doses of the toxin-antitoxin mixture plus killed suspension of *B. coli* were used during the 1927-28 season. This vaccine was issued to farmers through the veterinary profession and, though we have not been in personal touch with all farmers who used it, we are informed that the same good results as recorded in previous years have been got from its use.

We were able to arrange some experiments in which control uninoculated ewes were kept on the same farms as those inoculated; e.g. on Farm A in Table I 321 lambs were born, 157 from inoculated and 164 from uninoculated ewes. Table I is a summary of the results obtained in the South of Scotland, and shows that of 2,055 lambs born from inoculated ewes, 14 or 0·68 per cent. died of lamb dysentery, while of 2,442 lambs born from uninoculated control ewes on the same farms and lambing at the same time as those inoculated, 326 or 13·34 per cent. died. Table II records similar experiments carried out in Wales and shows that of 309 lambs born from 351 inoculated ewes, 4 or 1·3 per cent. died of lamb dysentery, while of 131 lambs born from 147 control uninoculated ewes, 15 or 11·4 per cent. died.

From such experiments we were satisfied that the vaccine made for the 1927-28 season had as good a protective value as that used in previous years. Inoculations were carried out as formerly, viz. one dose was injected in October or November before the ewes were pregnant, and a further dose in March or April about a fortnight before lambing was due to begin in the flock.

During the 1927-28 season we conducted experiments in the South of Scotland to ascertain (*a*) whether the killed suspension of *B. coli* was necessary in the vaccine and (*b*) whether good results would follow the use of a " toxoided " whole culture of the lamb dysentery anaerobe as a vaccine for ewe inoculation.

Experiments were carried out on 20 different farms, and during the whole of the lambing season, one of us (W.S.G.) visited each farm at frequent intervals and carried out *post-mortem* examinations on all lambs dying from all causes.

Toxin-antitoxin Without the Addition of B. coli.

The toxin-antitoxin mixture was made as already described[3] titration being carried out in mice by intravenous inoculations and tests for antigenic value in guinea-pigs. In all experimental work two groups of control ewes were kept (*a*) uninoculated control ewes and (*b*) ewes inoculated with toxin-antitoxin mixture plus *B. coli* suspension.

Table III shows the result of this experiment: Of 935 lambs born from ewes inoculated with the toxin-antitoxin without *B. coli* 10 or 1·07 per cent. died from lamb dysentery, while of 943 lambs born from ewes inoculated with the usual vaccine (toxin-antitoxin and *B. coli*), 8 or 0·84 per cent. died, and of 1,123 lambs born from ewes receiving no inoculation, 113 or 10·06 per cent. died. These results confirm the indications received from some small experiments carried out in 1926-27 that the presence of *B. coli* suspension in the vaccine is unnecessary.

" Toxoided " Whole Culture.

In the literature there are references to the use of " toxoided " whole culture in the establishing of immunity against some anaerobes. Lopez y Lopez[5], Cordier,[6] Karmann[7], Leclainche and Vallée[8], and M'Ewen[9], show that immunity can be produced against *B. chauvoei* and *Vibrion septique* by the use of such preparations.

We have carried out experiments which show that " toxoided " whole culture of the lamb dysentery anaerobe has as good a protective value as toxin-antitoxin mixture.

The " toxoided " whole culture is made by growing cultures of the anaerobe in meat broth. After filtration through sterile sand to remove the meat, 0·3 per cent. formalin (40 per cent. formaldehyde) is added to the filtrate which is kept at 37° C. till 0·5 c.c. just kills a mouse when injected intravenously while lower amounts fail to kill. Tests for antigenic value are carried out in guinea-pigs in the usual way. Ewes were inoculated with " toxoided " whole culture in the usual way and on all experimental farms two groups of controls were kept as in the above experiments. Table IV is a summary of the results of the experiment and shows that of 1,224 lambs born from ewes inoculated with " toxoided " whole culture, 13 or 1.06 per cent. died of lamb dysentery, while of 1,215 lambs born from ewes inoculated with the usual vaccine (toxin-antitoxin mixture with *B. coli*), 10 or 0·82 per cent. died, and of 1,333 lambs from uninoculated ewes, 191 or 14·33 per cent. died.

The Use of Antitoxin on Young Lambs.

Most of the 1928 experimental work with the antitoxin of the lamb dysentery anaerobe was carried out in Wales in collaboration with Dr. R. F. Montgomerie, Bangor, who kindly allowed one of his staff to perform the inoculations. *Post-mortem* examinations were carried out on all dead lambs and the diagnosis of lamb dysentery was based on the results. We are deeply indebted to Dr. Montgomerie for the accurate way in which these experiments were carried out and for the great interest he took in the work.

The results of the use of antitoxin in Wales are recorded in Table V. It will be noted that in the Llwyngwrill district no lamb receiving antitoxin died, while of 313 controls 65 or 20·76 per cent. died of lamb dysentery. It is of interest to note that on Farm B of the Meifod district, the only inoculated lamb dying of lamb dysentery was inoculated at a period later than 12 hours after birth.

Antitoxin was used in many districts in Scotland and England, and the general report is that the death rate among inoculated lambs was under 1 per cent. We are not in possession of all the details of inoculations carried out and doubtless on many farms no controls were kept.

Table VI has been prepared to show the results of an experiment carried out in collaboration with Mr. G. C. Inglis, M.R.C.V.S., Alloa. It will be noted that practically half the number of lambs born each day only were inoculated. The table shows that the result of the experiment is that of 320 inoculated lambs, 4 or 1·25 per cent. died of lamb dysentery, while of 298 uninoculated lambs, 61 or 20·47 per cent. died.

We are indebted to Mr. L. Llewelyn Jones, M.R.C.V.S., Llansantffraid, for the following particulars of the use of antitoxin on a farm in Montgomeryshire.

(*a*) 100 lambs were born before antitoxin was used—40 died of lamb dysentery.

(*b*) Antitoxin for 25 lambs was received—25 out of 40 lambs were inoculated. All inoculated lambs lived, while four of the 15 uninoculated died.

(*c*) A further supply of antitoxin for 40 lambs was received—40 out of 55 lambs were inoculated. No inoculated lamb died of lamb dysentery, while five of the 15 uninoculated died.

(*d*) During a period when no antitoxin was available, 60 lambs were born and of them 20 died of lamb dysentery.

(*e*) Antitoxin for 25 lambs was obtained—25 were inoculated and all lived.

(*f*) Two lambs born later were not inoculated and both died.

Summary and Conclusions.

(1) The inoculation of ewes with vaccine as used in former years (toxin-antitoxin of the lamb dysentery anaerobe plus killed *B. coli* suspension) has been again shown to give good results in protecting lambs against lamb dysentery.

(2) It has been shown that the addition of a killed suspension of *B. coli* is unnecessary from a protection standpoint.

(3) "Toxoided" whole culture of the lamb dysentery anaerobe used as a vaccine for ewe inoculation yields a high degree of protection against lamb dysentery in lambs.

(4) Antitoxin of the lamb dysentery anaerobe injected into young lambs prevents lamb dysentery in at least 99 per cent. of cases.

TABLE I.

Table showing comparison in death rate among lambs born from ewes inoculated with L.D. vaccine (T.A.M. + *B. coli*) and lambs born from uninoculated ewes.

Ewes all on the same farms and no selection made.

Farm.	Inoculated Ewes.			Uninoculated Ewes.		
	Lambs Born.	Lambs Died.	Per-centage.	Lambs Born.	Lambs Died.	Per-centage.
A	157	–	0·0	164	24	14·6
B	102	–	0·0	110	15	13·6
C	55	1	1·8	92	13	14·1
D	66	–	0·0	28	8	28·6
E	110	2	1·8	166	27	16·3
F	100	1	1·0	130	25	19·2
G	83	–	0·0	103	6	5·8
H	80	–	0·0	310	16	5·2
I	58	1	1·7	38	4	10·5
J	170	1	0·6	163	24	14·7
K	71	–	0·0	76	14	18·4
L	33	–	0·0	24	4	16·6
M	34	2	5·9	70	8	11·4
N	156	3	1·9	159	17	10·7
O	41	–	0·0	55	6	10·9
P	118	1	0·8	104	18	17·3
Q	90	–	0·0	90	16	17·7
R	96	1	1·0	104	13	12·5
S	79	–	0·0	75	8	10·6
T	58	1	1·7	54	18	33·3
U	48	–	0·0	58	14	24·1
V	48	–	0·0	54	5	9·3
W	80	–	0·0	37	7	18·9
X	72	–	0·0	118	9	7·6
Y	50	–	0·0	60	7	11·6
Total ...	2,055	14	0·68	2,442	326	13·34

Note.—The figures given in this table and those following are not selected; every farm under our control is included.

TABLE II.

Result of the Use of Vaccine on Ewes in Wales.

Farm.	Ewes Inoculated.	Lambs Born.	Died L.D.	Ewes Not Inoculated.	Lambs Born.	Died L.D.
A ...	55	60	1 (1·7%)	38	48	8 (16·7%)
B ...	151	132	1 (0·7%)	62	55	5 (9·1%)
C ...	145	117	2 (1·7%)	47	28	2 (7·1%)
Total	351	309	4 (1·3%)	147	131	15 (11·4%)

TABLE III.

Table showing comparison in death rate among lambs born from ewes inoculated with T.A.M. *without B. coli* and with T.A.M. *with B. coli* and lambs from uninoculated ewes.

Ewes all on same farms and no selection made.

	T.A.M. Alone.			T.A.M.+*B. coli*.			Uninoculated.		
Farm.	Lambs Born	Lambs Died L.D.	Percentage	Lambs Born	Lambs Died L.D.	Percentage	Lambs Born	Lambs Died L.D.	Percentage
A ...	102	1	1·0	102	–	0·0	110	15	13·6
B ...	94	1	1·1	108	2	1·8	97	3	3·1
C ...	90	2	2·2	100	1	1·0	130	25	19·2
D ...	55	–	0·0	58	1	1·7	38	4	10·5
E ...	55	1	1·9	58	1	1·7	51	2	3·9
F ...	30	–	0·0	21	–	0·0	57	2	3·5
G ...	31	–	0·0	30	–	0·0	63	1	1·6
H ...	31	1	3·2	34	2	5·9	70	8	11·4
I ...	54	1	1·9	41	–	0·0	55	6	10·9
J ...	97	1	1·0	90	–	0·0	90	16	17·7
K ...	89	2	2·3	96	1	1·0	104	13	12·5
L ...	80	–	0·0	83	–	0·0	80	2	2·5
M ...	83	–	0·0	72	–	0·0	118	9	7·6
N ...	44	–	0·0	50	–	0·0	60	7	11·6
Total	935	10	1·0	943	8	0·8	1,123	113	10·0

TABLE IV.

Table showing comparison in death rate among lambs born from ewes inoculated with " toxoided " whole culture and with T.A.M.+*B. coli* and lambs from uninoculated ewes.

Ewes all on the same farms and no selection made.

Farm.	Toxoided Whole Culture.			T.A.M.+*B. coli*.			Uninoculated.		
	Lambs Born.	Lambs Died.	Per-centage.	Lambs Born.	Lambs Died.	Per-centage.	Lambs Born.	Lambs Died.	Per-centage.
A ...	164	2	1·2	157	–	0·0	164	24	14·7
B ...	57	–	0·0	55	1	1·8	92	13	14·1
C ...	108	–	0·0	110	2	1·8	166	27	16·3
D ...	81	–	0·0	83	–	0·0	103	6	5·8
E ...	168	2	1·2	170	1	0·6	163	24	14·7
F ...	76	1	1·3	71	1	1·4	76	14	18·4
G ...	154	2	1·3	156	3	1·9	159	17	10·7
H ...	110	2	1·8	118	1	0·8	104	18	17·3
I ...	71	–	0·0	79	–	0·0	75	8	10·6
J ...	20	–	0·0	32	–	0·0	27	1	3·9
K ...	47	–	0·0	30	–	0·0	38	2	5·2
L ...	46	3	6·5	58	1	1·7	54	18	33·3
M ...	59	–	0·0	48	–	0·0	58	14	24·1
N ...	63	1	1·6	48	–	0·0	54	5	9·3
Total	1,224	13	1·06	1,215	10	0·82	1,333	191	14·33

TABLE V.

Use of Serum in the Prevention of Lamb Dysentery.

Every other Lamb born inoculated—Lambs inoculated within 12 hours of birth.

(a) *Llwyngwrill District.*

Farm.	Lambs Born.	Lambs Inoculated.	Died.	Lambs not Inoculated.	Died.	Percentage.
A ...	124	62	0	62	12	19·4
B ...	36	19	0	17	10	58·8
C ...	52	26	0	26	3	11·5
D ...	22	11	0	11	0	0·0
E ...	124	63	0	61	12	19·6
F ...	42	22	0	20	3	15·0
G ...	33	17	0	16	1	6·3
H ...	24	12	0	12	5	41·6
I ...	92	48	0	44	4	9·1
J ...	87	43	0	44	15	34·1
Total	636	323	0	313	65	20·76

(b) *Meifod District.*

Farm.	Lambs Born.	Lambs Inoculated.	Died.	Percentage.	Lambs not Inoculated.	Died.	Percentage.
A* ...	23	14	–	—	9	2	22·2
B ...	80	52	1†	1·9	28	8	28·6
Total	103	66	1	1·5	37	10	27·1

* This man keeps only 25 ewes; 12 lambs had been born before serum inoculation was started: of these 4 had died of L.D.

† Received serum later than 12 hours after birth.

TABLE VI.

DETAILS OF THE RESULTS OF INOCULATION OF LAMBS WITH SERUM ON ONE FARM.

Date.	Lambs Born.	Lambs Inoculated.	Died L.D.	Lambs not Inoculated.	Died L.D.
April 8 ...	12	6	–	6	–
9 ...	20	10	–	10	–
10 ...	25	13	–	12	1
11 ...	32	16	–	16	3
12 ...	30	15	–	15	1
13 ...	36	18	–	18	3
14 ...	32	16	–	16	4
15 ...	40	20	1	20	5
16 ...	45	23	–	22	3
17 ...	44	22	–	22	4
18 ...	37	20	1	17	4
19 ...	49	29	–	20	6
20 ...	55	30	–	25	3
21 ...	45	25	–	20	2
22 ...	40	20	1	20	4
23 ...	36	20	–	16	3
24 ...	40	17	–	13	2
25 ...	—	—	–	—	3
26 ...	—	—	–	—	4
27 ...	—	—	1	—	3
28 ...	—	—	–	—	2
29 ...	—	—	–	—	1
Total ...	618	320	4=1·25%	298	61=20.47%

REFERENCES

(1) Dalling, Mason and Gordon. *Veterinary Record*, 1928, June 30th, p. 532.
(2) Dalling, Allen and Mason. *Veterinary Record*, 1925, July 11th, p. 561.
(3) Dalling, T. *Journ. Comp. Path. and Therp.*, 1926, Vol. XXXIX, p. 148.
(4) Dalling, Mason and Gordon. *Journ. Comp. Path. and Therap.*, 1927, Vol. XL, Part 3, p. 217.
(5) Lopez y Lopez. *Revista de Higiene e Sanidad pecuarias*, 1926, January.
(6) Cordier, G. *Comptes rendus de la Societe de Biologie*, 1926, 95, p. 848.
(7) Karmann, P. *Zeitschrift fur Infektionsk. der Haustiere*, 1927, 31, p. 226.
(8) Leclainche and Vallée. *Rev. Gen. de Med. Vet.*, 1928, Feb. 15th, No. 434, p. 65.
(9) M'Ewen, A. D. *Journ. Comp. Path and Therap.*, 1926, Vol. 39, p. 253.

VALUE OF VACCINATION AGAINST BLACK QUARTER.

By G. H. LEADER, M.R.C.V.S.,
Bridgnorth, Salop.

On November 20th a client left a message that he had a young heifer which he suspected of having foot-and-mouth disease (lameness, excessive salivation, etc.), and he wished me to go out immediately.

On arrival I found a heifer calf about eight or nine months old dead, but she had obviously only just died. The history and appearances of the body were absolutely typical of any case of black quarter except in one respect, and that was the tongue. There was a lesion developing in the muscles of the leg which she had been lame on (no sign whatever of foot-and-mouth as at first suspected by the owner), soreness of the part, etc., and death within a few hours of the onset of symptoms.

And now I come to the interesting point: the tongue was enormously swollen and typical of what one would expect to see if it had a blackleg lesion developing in it. It showed all the characteristics of such a lesion and the swelling was so bad that I would not care to say whether death was the result of the disease or of asphyxiation.

On inquiry I discovered that some of these calves had not been vaccinated this year (including this one) and I know the farm to be a noted one for black quarter. I treated the remainder with agressin the following day and have had no more trouble since.

I have been trying since then to find a similar case reported or to discover mention of blackleg affecting the tongue, but I cannot do so up to now.

I feel confident that that was what it was, and although it never occurred to me before it has since struck me to wonder why more cases of this type are not found, since one of the probable methods of infection with blackleg is by ingestion and at that age young animals are likely to have abrasions of the gums from the shedding of teeth.